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EXPERIMENTS ON ANIMALS

EXPERIMENTS ON ANIMALS

By Stephen Paget

WITH AN INTRODUCTION
BY LORD LISTER

Semper ego auditor tantum, nunquamne reponam
Vexatus toties?

New York:
WILLIAM WOOD & COMPANY
1900

TO

CHARLES ALFRED BALLANCE, M.S., F.R.C.S.,

AND

WILLIAM HUNTER, M.D., F.R.C.P.

F45
P13
1900

PREFACE

FOR twelve years it was the writer's business, as secretary to the Association for the Advancement of Medicine by Research, to know something about experiments on animals, and to follow the working of the Act of 1876; and to give facts and references to a very large number of applicants. Believing that an account of these experiments, and of the conditions imposed upon them by the Act, might serve a useful purpose, he proposed to the Council of the Association that he should write a book on the subject. The Council accepted this proposal; and decided that the book should be written for general reading, that it should not be anonymous, and that it should be published without reserve.

It was of course a doubtful and embarrassing task. But, from twelve years' experience of the things that are said by the chief opponents of all experiments on animals, he knew that there was only one way of doing it—to give the original authorities, the plain facts, the very words, chapter and verse for everything.

Among those who kindly revised the proofs were Dr. Rose Bradford and Prof. Starling, who revised Part I.; Mr. Shattock, who revised Part II.; and Prof. Schäfer. Certain valuable reports, references, and illustrations, were contributed by Mr. R. H. Clarke, Mr. Horsley, Dr. Washbourn, Dr. Beevor, and Surgeon-Major Ross.

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INTRODUCTION

THIS work by Mr. Paget is entirely a labour of love. Not being himself engaged in researches involving experiments upon the lower animals, he is not directly interested in the subject. But, in his official capacity as Secretary to the Association for the Advancement of Medicine by Research, he has become widely conversant with such investigations, and has been deeply impressed with the greatness of the benefits which they have conferred upon mankind, and the grievous mistake that is made by those who desire to suppress them.

The action of these well-meaning persons is based upon ignorance. They allow that man is permitted to inflict pain upon the lower animals when some substantial advantage is to be gained; but they deny that any good has ever resulted from the researches which they condemn.

How far such statements are from the truth will be evident to those who peruse this book. Its earlier pages deal with Physiology, the main basis of all sound medicine and surgery. The examples given in this department are not numerous; they are, however, sufficiently striking, as indications that, from the discovery of the circulation of the blood onwards, our knowledge of healthy animal function has been mainly derived from experiments on animals.

The chief bulk of the work is devoted to the class of investigations which are most frequent at the present day; and it shows what a flood of light has been already thrown by Bacteriology upon the nature of human disease and the means of combating it.

The chapter on the Action of Drugs will be to many a startling disclosure of the gross ignorance that prevailed among physicians even in the earlier part of last century. The great revolution that has since taken place is no doubt largely due to advances in sciences other than Biology, especially Chemistry. But it could not have attained its present proportions without the ever-increasing knowledge of Physiology, based on experiments on animals; and Mr. Paget shows how large a share these have had in the direct investigation of articles of the Materia Medica.

The concluding part of the volume discusses the restrictions which have been placed by the legislature in this country on those engaged in these researches, with the view of obviating possible abuse. Whether the Act in question has been really useful, whether it has not done more harm than good, by hampering and sometimes entirely preventing legitimate and beneficent investigation, I will not now discuss.

Meanwhile I commend Mr. Paget's book to the careful consideration of the reader.

LISTER.

EXPERIMENTS IN PHYSIOLOGY

I

THE BLOOD

I

Before Harvey

GALEN, born at Pergamos, 131 A.D., proved by experiments on animals that the brain is as warm as the heart, against the Alexandrian doctrine that the office of the brain was to keep the heart cool. He also proved that the arteries during life contain blood, not πνεῦμα, the breath of life :—

> "Ourselves, having tied the exposed arteries above and below, opened them between the ligatures, and showed that they were indeed full of blood."

Though all vessels bleed when they are wounded, yet this experiment was necessary to refute the fanciful teaching of Erasistratus and his followers :—

> "Erasistratus is pleased to believe that an artery is a vessel containing the breath of life, and a vein is a vessel

containing blood; and that the vessels, dividing again and again, come at last to be so small that they can close their ultimate pores, and keep the blood controlled within them; yea, though the pores of the vein and of the artery lie side by side, yet the blood remains within its proper bounds, nowhere passing into the vessels of the breath of life. But when the blood is driven with violence from the veins into the arteries, forthwith there is disease; and the blood is poured the wrong way into the arteries, and there withstands and dashes itself against the breath of life coming from the heart, and turns the course of it—and this forsooth is fever."

From Galen to the Renaissance, physiology made no great advance, for want of experiments. Of Servetus, Cæsalpinus, and Ruinius, Harvey's near predecessors, this much only need be said here, that they did not discover the circulation of the blood. Realdus Columbus (1559) understood its passage through the lungs, but not the general circulation:—

"The blood is carried through the pulmonary artery to the lung, and there is attenuated; thence, mixed with air, it is carried through the pulmonary vein to the left ventricle of the heart. Which thing no man hitherto has noted or left on record, though it is most worthy of the observance of all men. . . . And this is as true as truth itself; for if you will look not only in the dead body but also in the living animal, you will always find this pulmonary vein full of blood, which assuredly it would not be, if it were designed only for air and vapours. . . . Verily I pray you, O candid reader, studious of authority, but more studious of truth, to make experiment on animals. You will find the pulmonary vein full of blood, not air or *fuligo*, as these men call it, God help them. Only there is no pulsation in the vein." (*De Re Anatomicâ*, Venice, 1559.)

Fabricius ab Aquapendente, Harvey's master at Padua, published his work on the valves of the veins—*De Venarum Ostiolis*—in 1603. He did not discover them. Sylvius speaks of them in his *Isagoge* (Venice, 1555), and they were known to Amatus (1552), and even to Theodoretus, Bishop of Syria, who lived, as John Hunter said of Sennertus, "the Lord knows how long ago." But Fabricius studied them most carefully; and in anatomy he left nothing more to be said about them. In physiology, his work was of little value; for he held that they were designed "to retard the blood in some measure, lest it should run pell-mell into the feet, hands, and fingers, there to be impacted:" they were to prevent distension of the veins, and to ensure the due nourishment of all parts of the body. It is true that he compared them to the locks or weirs of a river, but he understood neither the course nor the force of the blood: as Harvey said of him, "The man who discovered these valves did not rightly understand their use; neither did they who came after him."[1] Men had no idea of the rapidity and volume of the circulation; they thought of a sort of Stygian tide, oozing this way or that way in the vessels—Cæsalpinus was of opinion that it went one way in the daytime and another at night—nor did they see that the pulmonary circulation and the general circulation are one system, the same blood covering the whole course.

---

[1] "Clarissimus Hieronymus Fabricius ab Aquapendente, peritissimus anatomicus et venerabilis senex, vel (ut voluit doctissimus Riolanus) Jacobus Silvius, primus in venis membraneas valvulas delineavit. . . . Harum valvularum usum rectum inventor non est assecutus, nec alii addiderunt; non est enim ne pondere deorsum sanguis in inferiora totus ruat; sunt namque in jugularibus deorsum spectantes, et sanguinem sursum ferri prohibentes." (Harvey, *De Motu Cordis*.)

II

Harvey (1578–1657)

The *De Motu Cordis et Sanguinis in Animalibus* was published at Frankfort, in 1621. And it begins with these words—*Cum multis vivorum dissectionibus, uti ad manum dabantur*:—

"When by many dissections of living animals, as they came to hand, I first gave myself to observing how I might discover, with my own eyes, and not from books and the writings of other men, the use and purpose of the movement of the heart in animals, forthwith I found the matter hard indeed, and full of difficulty: so that I began to think, with Frascatorius, that the movement of the heart was known to God alone. For I could not distinguish aright either the nature of its systole and diastole, nor when nor where dilatation and contraction took place; and this because of the swiftness of the movement, which in many animals in the twinkling of an eye, like a flash of lightning, revealed itself to sight and then was gone; so that I came to believe that I saw systole and diastole now this way now the other, and movements now apart and now together. Wherefore my mind wavered; I had nothing assured to me, neither decided by me nor taken from other men : and I did not wonder that Andreas Laurentius had written that the movement of the heart was what the ebb and flow of the Euripus had been to Aristotle.

"At last, having daily used greater disquisition and diligence, by frequent examination of many and various living animals, and many observations put together, I came to believe that I had succeeded, and had escaped and got out of this labyrinth, and therewith had discovered what I desired, the movement and use of the heart and the arteries. And from that time, not only to my friends, but also in public in my anatomical lectures, after the manner of the Academy, I did not fear to set forth my opinion in this matter."

It is plain, from Harvey's own words, that he gives to experiments on animals the first place among his methods of work. Take only the headings of his first four chapters :—

i. *Causæ, quibus ad scribendum auctor permotus fuerit.*
ii. *Ex vivorum dissectione, qualis fit cordis motus.*
iii. *Arteriarum motus qualis, ex vivorum dissectione.*
iv. *Motus cordis et auricularum qualis, ex vivorum dissectione.*

He thrusts it on us, he puts it in the foreground. Read the end of his Preface :—

"Therefore from these and many more things of the kind, it is plain (since what has been said by men before me, of the movement and use of the heart and arteries, appears inconsistent or obscure or impossible when one carefully considers it) that we shall do well to look deeper into the matter ; to observe the movements of the arteries and the heart, not only in man, but in all animals that have hearts ; and by frequent dissection of living animals, and much use of our own eyes, to discern and investigate the truth."

Finally, take the famous passage in the eighth chapter, *De copiâ sanguinis transeuntis per cor e venis in arterias, et de circulari motu sanguinis* :—

"And now, as for the great quantity and forward movement of this blood on its way, when I shall have said what things remain to be said—though they are well worth considering, yet they are so new and strange that I not only fear harm from the envy of certain men, but am afraid lest I make all men my enemies ; so does custom, or a doctrine once imbibed and fixed down by deep roots, like second nature, hold good among all men, and reverence for antiquity constrains them. Be that as it may, the die is cast now : my hope is in the love of truth, and the candour of learned minds. I bethought me how great was the quantity of this blood. Both from the dissection of living animals for the sake of experiment, with opening of the arteries, with observations manifold ; and from the symmetry and size of the ventricles and of the vessels entering and leaving the heart—because Nature, doing nothing in vain, cannot in vain have given such size to these vessels above the rest—and from the harmonious and happy device of the valves and fibres, and all other fabric of the heart ; and from many other things—when I had again and again carefully considered it all, and had turned it over in my mind many times—I mean the great quantity of the blood passing through, and the swiftness of its passage—and I did not see how the juices of the food in the stomach could help the veins from being emptied and drained dry, and the arteries contrariwise from being ruptured by the excessive flow of blood into them, unless blood were always getting round from the arteries into the veins, and so back to the right ventricle—I began to think to myself whether the blood had a certain movement as in a circle, which afterward I found was true."

Those who are opposed to all experiments on animals do not hesitate to assure Harvey that he was wrong in saying that these experiments helped him: really, they only confused him. Mr. Berdoe, in the *Zoophilist* for July, 1899, says—

> "I will give you his (Harvey's) exact words—'At length, and by using greater and daily diligence and investigation, making frequent inspection of many and various animals, and collating numerous observations, I thought that I had attained to the truth.' You see he says 'frequent inspection' of many animals, and collating 'numerous observations.' *I take it this means anatomical dissections*, descriptions of which occupy a great portion of his book."

Mr. Berdoe here quotes Bowie's translation (1889). Harvey's exact words are, *Multa frequenter et varia animalia viva introspiciendo.* The translator left out *viva.*

Mr. Abiathar Wall, in an essay written against experiments on animals, quotes the opening sentences of Harvey's book, *When by many dissections . . . . had been to Aristotle;* there he stops quoting, and goes on thus—*Perplexed and baffled, Harvey then went back to examining the anatomy of the dead body.*

And Mr. Adams, in a book called *The Coward Science*, simply says—*Both Harvey and Hunter state plainly the manner in which their respective discoveries were suggested. In neither case are these discoveries ascribed to vivisection.*

There is yet another way of telling Harvey that he did not know what he was talking about: there is Sir Robert Boyle's letter :—

> "I remember that when I asked our famous Harvey, *in the only discourse I had with him, which was but a while before he died*, what were the things which induced him to think of the circulation of the blood, he answered me that when he took notice that the valves in the veins of so many parts of the body were so placed that they gave free passage of the blood towards the heart, but opposed the passage of the venal blood the contrary way, he was invited to imagine that so provident a cause as Nature had not so placed so many valves without design; and no design seemed more probable than that, since the blood could not well, because of the interposing valves, be sent by the veins to the limbs, it should be sent by the arteries, and return through the veins; whose valves did not oppose its course that way."

And this letter has been quoted against all experiments on animals, without the words *in the only discourse . . . . before he died.* Which makes a difference: for Harvey lived to fourscore years—"an old man far advanced in years and occupied with other cares." So he spoke of himself. Moreover, Sir Robert Boyle only says that anatomy suggested something to him, invited him to imagine something, gave him a theory. And it is stupid, or worse than stupid, to attempt to set this letter against Harvey's exact words.

III

AFTER HARVEY

1. *The Capillaries.*

The capillary vessels were not known in Harvey's time: the *capillamenta* of Cæsalpinus were not the capillaries, but the νεῦρα of Aristotle. The first account of the capillaries is in two letters *De Pulmonibus*, 1661, from Malpighi, professor of medicine at Bologna, to Borelli, professor of mathematics at Pisa. It has been said, in an off-hand way, that anybody could have discovered the circulation with a dead body and an injecting syringe. That is just what Malpighi tried. He says, in his first letter—

> "This enigma hitherto distracts my mind, though for its solution I have made many and many attempts, all in vain, with air and various coloured fluids. Having injected ink with a syringe into the pulmonary artery, I have again and again seen it escape at several points. The same thing happens with an injection of mercury. These experiments do not give us the natural pathway of the blood."

But in his second letter he writes that he has examined, with a microscope of two lenses, the lung and the mesentery of a frog, and has seen the capillaries, and the blood in them :--

> "Such is the divarication of these little vessels, coming off from the vein and the artery, that the order in which the vessel ramifies is no longer preserved, but it looks like a network woven from the offshoots of both vessels."

But, in spite of the work of Malpighi, Leeuwenhoek, and others, it took nearly half a century before Harvey's teaching was believed by all men—*Tantum consuetudo apud omnes valet.*

2. *The Blood-pressure.*

Harvey had seen the facts of blood-pressure—*the great quantity of blood passing through, and the swiftness of its passage*—but he had not measured it. Keill's experiments on the blood-pressure (1718) were inexact and of no value : and the first exact measurements were made by Stephen Hales, who was rector of Farringdon and minister of Teddington, and a Fellow of the Royal Society. In 1733, he published, in two volumes, his *Statical Essays containing Hæmostaticks : or an Account of some Hydraulick and Hydrostatical Experiments made on the Blood and Blood-vessels of Animals* :—

> "Finding but little satisfaction in what had been attempted on this subject by Borellus and others, I

endeavoured about twenty-five years since, by proper experiments, to find what was the real force of the blood in the crural arteries of dogs, and about six years afterwards I repeated the like experiments on two horses, and a fallow doe ; but did not then pursue the matter any further, being discouraged by the disagreeableness of anatomical dissections. But having of late years found by experience the advantage of making use of the statical way of investigation, not only in our researches into the nature of vegetables, but also in the chymical analysis of the air ; I was hence induced to hope for some success, if the same method of enquiry were applied to animal bodies."

He then gives an account of the famous experiment where he measured, in a vertical glass tube, the blood-pressure in the crural artery of a mare.

3. *Collateral Circulation.*

After Hales, came John Hunter, who was five years old when the *Statical Essays* were published. His experiments on the blood were mostly concerned with its properties, not with its course ; but one great experiment must be noted here, that puts him in line with Harvey, Malpighi, and Hales. He got from it his knowledge of the collateral circulation : how the obstruction of an artery is followed by enlargement of the vessels in its neighbourhood, so that the parts beyond the obstruction shall not suffer from want of blood : and the facts of collateral circulation were fresh in his mind when, a few months later, he conceived and performed his operation for aneurysm (December, 1785). The "old operation" gave him no help here; and "Anel's operation" was but a single instance, and no sure guide for Hunter, because Anel's patient had a different sort of aneurysm. Hunter knew that the collateral circulation could be trusted to nourish the limb, if the femoral artery were ligatured in "Hunter's canal" for the cure of popliteal aneurysm; and he got this knowledge from the experiment that he had made on one of the deer in Richmond Park, to see the influence of ligature of the carotid artery on the growth of the antler. The following account of this experiment was given by Sir Richard Owen, who had it from Mr. Clift, Hunter's devoted pupil and friend:—

> "In the month of July, when the bucks' antlers were half-grown, he caused one to be caught and thrown; and, knowing the arterial supply to the hot 'velvet' as the keepers call it, Hunter cut down upon and tied the external carotid; upon which, laying his hand upon the antler, he found that the pulsations of the arterial channels stopped, and the surface soon grew cold. The buck was released, and Hunter speculated on the result—whether the antler, arrested at midgrowth, would be shed like the full-grown one, or be longer retained. A week or so afterward, he drove down again to the park, and caused the buck to be caught and thrown. The wound was healed about the ligature; but on laying his hand on the antler, he found to his surprise that the warmth had returned, and the channels of supply to the velvety forma-

tive covering were again pulsating. His first impression was that his operation had been defective. To test this, he had the buck killed and sent to Leicester Square. The arterial system was injected. Hunter found that the external carotid had been duly tied. But certain small branches, coming off on the proximal or heart's side of the ligature, had enlarged; and, tracing-on these, he found that they had anastomosed with other small branches from the distal continuation of the carotid, and these new channels had restored the supply to the growing antler. . . . . Here was a consequence of his experiment he had not at all foreseen or expected. A new property of the living arteries was unfolded to him: capillaries can enlarge according to a 'stimulus of necessity.'"

All the anatomists, from Vesalius onward, had overlooked this physiological change in the living body, brought about by disease. And the surgeons, since anatomy could not help them, had been driven by the mortality of the "old operation" to the practice of amputation.

To Hunter's study of the collateral circulation and of aneurysm must be added all his work on the nature and properties of the blood itself.

After Hunter, came the use of the mercurial manometer (Poiseuille, 1828, and Ludwig, 1847), for a more accurate estimate of the blood-pressure than Hales had attempted; the observations on the sounds of the heart, made by sub-committees of the British Association (1835–1840); Hering's work on the endocardial pressure (1849); and the use of recording instruments by Volckmann (1850) and Chauveau and Marey (1863), for obtaining permanent tracings of the pressure-curves. Afterward came the use of the sphygmograph in practice. Finally, after the discovery of the vaso-motor nerves, and with the advance of physics and organic chemistry, came the study of those more abstruse problems of the circulation that the older physiologists had not so much as considered: the multiple influences of the central nervous system, the relations between blood-pressure and secretion, the automatism of the heart-beat, the influence of gravitation, and other finer and more complex issues of physiology.

II

THE LACTEALS

THE lacteal vessels in the mesentery were seen long ago, but not understood. Both Galen and Erasistratus had observed the milk-white threads, filled with chyle; but had not traced them to the thoracic duct, that carries their contents into a vein near the heart. The lacteals, without the thoracic duct, were like a riddle without its answer; and from the time of Galen down to the time of Harvey, men failed to study them. What Galen and Erasistratus had seen, Asellius and Pecquet discovered; and Harvey gives a careful review of this discovery in his letters to Nardi (May, 1652) and to Morison (November, 1653). He does not accept it; but the point is that he recognises it as a new thing, a discovery. Asellius (1622), by a single experiment, demonstrated the flow of chyle, and brought men to see the facts about it:—

> "I observed that the nerves of the intestines were quite distinct from these white threads, and ran a different course. *Struck with this new fact, I was silent for a time, thinking of the bitter warfare of words among anatomists*, as to the mesenteric veins and their purposes. *When I came to myself, to satisfy myself by an experiment*, I pierced one of the largest cords with a scalpel. I hit the right point, and at once observed a white liquid like milk flowing from the divided vessel."

And he goes on to describe his pleasure at the wonderful sight: how he cried Eureka, and called his friends to see it.

Jehan Pecquet (1647), in the course of an experiment on the heart, observed the flow of chyle into the subclavian vein, and its identity with the chyle in the lacteals: and, by further experiment, he found the thoracic duct, and the chyle flowing up it:—

> "I perceived a white substance, like milk, flowing from the vena cava ascendens into the pericardium, at the place where the right auricle had been. . . . I found these vessels (the thoracic duct) all along the dorsal vertebræ, lying on the spine, beneath the aorta. They swelled below a ligature; and when I relaxed it, I saw the milk carried to the orifices that I had observed in the subclavian veins."

The *Zoophilist* says that "Aselli died in ignorance of the true bearing of his discovery. And twenty years later the anatomist Pecquet blew the theories of the vivisectionists to the winds." But here are Jehan Pecquet's exact words. And what he found had been overlooked by Vesalius and all the great anatomists of the Renaissance.

III

THE GASTRIC JUICE

THE following account of the first experiments on digestion is taken from Claude Bernard's *Physiologie Opératoire*, 1879 :—

"The true experimental study of digestion is of comparatively recent date ; the ancients were content to find comparisons, more or less happy, with common facts. Thus, for Hippocrates, digestion was a 'coction' : for Galen, a 'fermentation' as of wine in a vat. In later times, van Helmont started this comparison again : for him, digestion was a fermentation like that of bread : as the baker, having kneaded the bread, keeps a little of the dough to leaven the next lot kneaded, so, said van Helmont, the intestinal canal never completely empties itself, and the residue that it keeps after each digestion becomes the leaven that shall serve for the next digestion.

"The first experimental studies on the digestion date from the end of the seventeenth century, when the Academy of Florence was the scene of a famous and long controversy between Borelli and Valisńieri. The former saw nothing more in digestion than a purely mechanical act, a work of attrition whereby the ingesta were finely divided and as it were pulverised : and in support of this opinion Borelli invoked the facts that he had observed relating to the gizzard of birds. We know that this sac, with its very thick muscular walls, can exercise on its contents pressure enough to break the hardest bodies. Identifying the human stomach with the bird's gizzard, Borelli was led to attribute to the walls of the stomach an enormous force, estimated at more than a thousand pounds ; whose action, he said, was the very essence of digestion. Valisnieri, on the contrary, having had occasion to open the stomach of an ostrich, had found there a fluid which seemed to act on bodies immersed in it ; this fluid, he said, was the active agent of digestion, a kind of *aqua fortis* that dissolved food.

"These two opposed views, resulting rather from observations than from regularly instituted experiments, were the starting-point of the experimental researches undertaken by Réaumur in 1752. To resolve the problem set by Borelli and Valisnieri, Réaumur made birds swallow food enclosed in fenestrated tubes, so that the food, protected from the mechanical action of the walls of the stomach, was yet exposed to the action of the gastric fluid. The first tubes used (glass, tin, &c.) were crushed, bent, or flattened by the action of the walls of the gizzard ; and Réaumur failed to oppose to this force a sufficient resistance, till he employed leaden tubes thick enough not to be flattened by a pressure of 484 pounds : which was, in fact, the force exercised by the contractile walls of the gizzard in turkeys, ducks, and fowls under observation. These leaden tubes—filled with ordinary grain, and closed only by a netting that let pass the gastric juices—these tubes, after a long stay in the stomach, still enclosed grain wholly intact, if it had not been crushed before the experiment. When they were filled with meat it was found changed, but not digested. Réaumur was thus led at first to consider digestion, in the gallinaceæ, a pure and simple trituration. But, repeating these experiments on birds ot prey, he observed that digestion in them consists essentially in dissolution, without any especial mechanical action, and that it is the same with the digestion of meat in all animals with membranous stomachs. To procure this dissolving fluid, Réaumur made the birds swallow sponges with threads attached : withdrawing these sponges after a definite period, he squeezed the fluid into a glass, and tested its action on meat. That was the first attempt at artificial digestion *in vitro*. He did not carry these last investigations very far, and did not obtain very decisive results : nevertheless he must be considered as the discoverer of artificial digestion."

After Réaumur, the Abbé Spallanzani (1777) made similar observations on many other animals, including carnivora. He showed that even in the gallinaceæ there was dissolution of food, not mere trituration : and observed how after death the gastric fluid may under certain conditions act on the walls of the stomach itself.

"Henceforth the experimental method had cut the knot of the question raised by the theories of Borelli and Valisnieri : digestion could no longer be accounted anything but a dissolution of food by the fluid of the stomach, the gastric juice. But men had still to understand this gastric juice, and to determine its nature and mode of action. Nothing could be more contradictory than the views on this matter. Chaussier and Dumas, of Montpellier, regarded the gastric juice as of very variable composition, one time alkaline, another acid, according to the food ingested. Side by side with these wholly theoretical opinions, certain results of experiments had led to ideas just as erroneous, for want of rigorous criticism of methods; it was thus that Montègre denied the existence of the gastric juice as a special fluid; what men took for gastric juice, he said, was nothing but the saliva turned acid in the stomach. To prove his point, he made the following experiment: he masticated a bit of bread, then put it out on a plate: it was at first alkaline, then at the end of some time it became acid. In those days (1813) this experiment was a real embarrassment to the men who believed in the existence of a special gastric juice: we have now no need to refute it.

"These few instances suffice to show how the physiologists were unsettled as to the nature and properties of the gastric juice. Then (1823) the Academy had the happy idea of proposing digestion as a subject for a prize. Tiedemann and Gmelin in Germany, Leuret and Lassaigne in France, submitted works of equal merit, and the Academy divided the prize between them. The work of Tiedemann and Gmelin is of especial interest to us on account of the great number of their experiments, from which came not only the absolute proof of the existence of the gastric juice, but also the study of the transformation of starch into glucose. Thus the theory of digestion entered a new phase: it was finally recognised, at least for certain substances, that digestion is not simply dissolution, but a true chemical transformation." (Cl. Bernard, *loc. cit.*)

In 1825 Dr. William Beaumont, a surgeon in the United States army, began his famous experiments on Alexis St. Martin, a young Canadian travelling for the American Fur Company, who was shot in the abdomen on June 6, 1822, and recovered, but was left with a permanent opening in his stomach. Since the surgery of those days did not favour an operation to close this fistula, Dr. Beaumont took St. Martin into his service, and between 1825 and 1833 made a vast number of experiments on him. These he published,[1] and they were of great value. But, for the purpose of this book, it is to be noted that the ground had been cleared already, fifty years before, by Réaumur and Spallanzani :—

> "*I make no claim to originality in my opinions*, as it respects the existence and operation of the gastric juice. My experiments confirm the doctrines (with some modifications) taught by Spallanzani, and many of the most enlightened physiological writers." (Preface to Dr. Beaumont's book.)

Further, it is to be noted that Alexis St. Martin's case proves that a gastric fistula is not painful. Scores of experiments were made on him, off and on, for nine years :—

> "During the whole of these periods, from the spring of 1824 to the present time (1833), he has enjoyed general good health, and perhaps suffered much less predisposition to disease than is common to men of his age and circumstances in life. He has been active, athletic, and vigorous; exercising, eating, and drinking like other healthy and

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[1] *Experiments and Observations on the Gastric Juice, and the Physiology of Digestion.* By William Beaumont, M.D. Edinburgh, 1838.

active people. For the last four months he has been unusually plethoric and robust, though constantly subjected to a continuous series of experiments on the interior of the stomach; allowing to be introduced or taken out at the aperture different kinds of food, drinks, elastic catheters, thermometer tubes, gastric juice, chyme, &c., almost daily, and sometimes hourly.

"Such have been this man's condition and circumstances for several years past; and he now enjoys the most perfect health and constitutional soundness, with every function of the system in full force and vigour." (Dr. Beaumont, *loc. cit.*, p. 20.)

In 1834 Eberlé published a series of observations on the extraction of gastric juice from the mucous membrane of the stomach after death; in 1842 Blondlot of Nancy studied the gastric juice of animals by the method of a fistula, such as Alexis St. Martin had offered for Dr. Beaumont's observation. After Blondlot, came experiments on the movements of the stomach, and on the manifold influences of the nervous system on digestion.

It has been said, times past number, that an animal with a fistula is in pain. It is not true. The case of St. Martin is but one out of a multitude of these cases: an artificial orifice of this kind is not painful.

IV

GLYCOGEN

CLAUDE BERNARD'S discovery of glycogen in the liver had a profound influence both on physiology and on pathology. Take first its influence on pathology. Diabetes was known to Celsus, Aretæus, and Galen; Willis, in 1674, and Morton, in 1675, noted the distinctive sweetness of the urine; and their successors proved the presence of sugar in it. Rollo, in 1787, observed that vegetable food was bad for diabetic patients, and introduced the strict use of a meat diet. But Galen had believed that diabetes was a disease of the kidneys, and most men still followed him: nor did Rollo greatly advance pathology by following not Galen, but Aretæus. Later, with the development of organic chemistry, came the work of Chevreuil (1815), Tiedemann and Gmelin (1823), and other illustrious chemists: and the pathology of diabetes grew more and more difficult:—

> "These observations gave rise to two theories : the one, that sugar is formed with abnormal rapidity in the intestine, absorbed into the blood, and excreted in the urine ; the other, that diabetes is due to imperfect destruction of the sugar, either in the intestine or in the blood. Some held that it underwent conversion into lactic acid as was passing through the intestinal walls, while others believed it to be destroyed in the blood by means of the alkali therein contained." [1]

Thus, before Claude Bernard (1813–1878), the pathology of diabetes was almost worthless. And, in physiology, his work was hardly less important than the work of Harvey. A full account of it, in all its bearings, is given in Sir Michael Foster's *Life of Claude Bernard* (Fisher Unwin, 1899).

In his *Leçons sur le Diabète et la Glycogenèse Animale* (Paris, 1877), there is a sentence that has been misquoted many times :—

> *Sans doute, nos mains sont vides aujourd'hui, mais notre bouche peut être pleine de légitimes promesses pour l'avenir.*

This sentence has been worked so hard that some of the words have got rubbed off it : and the statement generally made is of this kind :—

> *Claude Bernard himself confessed that his hands were empty, but his mouth was full of promises.*

Of course, he did not mean that he was wrong in his facts. But, in this particular lecture, he is speaking of the want of more science in practice, looking forward to a time when treatment should be based on science, not on tradition. Medicine, he says, is neither science nor art. Not science—*Trouverait-on aujourd'hui un seul médecin raisonnable et instruit osant dire qu'il prévoit d'une manière certaine la marche et l'issue d'une maladie ou l'effet d'une remède?* Not art, because art has always something to show for its trouble: a statue, a picture, a poem—*Le médecin artiste ne crée rien, et ne laisse aucune œuvre d'art, à moins d'appliquer ce titre à la guérison du malade. Mais quand le malade meurt, est-ce également son œuvre? Et quand il guérit, peut-il distinguer sa part de celle de la nature?*

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[1] *Reynolds' System of Medicine*, vol. v. : Art., Diabetes Mellitus.

To Claude Bernard, experiments on animals for the direct advancement of medicine seemed a new thing: new, at all events, in comparison with the methods of some men of his time. He was only saying what a great English physiologist had said in 1875 to the Royal Commission:—

> *It is my profound conviction that a future will come, it may be a somewhat distant future, in which the treatment of disease will be really guided by science. Just as completely as mechanical science has come to be the guide of the mechanical arts, do I believe, and I feel confident, that physiological science will eventually come to be the guide of medicine and surgery.*

Anyhow, lecturing a quarter of a century ago on diabetes, his special subject, Claude Bernard spoke out his longing to compel men into the ways of science, to give them some immediate sign which they could not refuse to see :—

"At this present time, medicine is passing from one period to another. The old traditions are losing ground, and scientific medicine (*la médecine expérimentale*) has got hold of all our younger men : every day it gains ground, and will establish itself against all its critics, and in spite of the excesses of those who are over-zealous for its honour. . . . And when men ask us what are the results of scientific medicine, we are driven to answer that it is scarcely born, that it is still in the making. Those who care for nothing but an immediate practical application must remember Franklin's words, *What is the use of a new-born child, but to become a man?* If you deliberately reject scientific medicine, you fail to see the natural development of man's mind in all the sciences. Without doubt, our hands are empty to-day, but our mouth may well be filled with legitimate promises for the future."

He died in 1878. The following account of his discovery of glycogen is taken from his *Nouvelle Fonction du Foie* (Paris, 1853) :—

"My first researches into the assimilation and destruction of sugar in the living organism were made in 1843 : and in my inaugural thesis (Dec., 1843) I published my first experiments on the subject. I succeeded in demonstrating a fact hitherto unknown, that cane-sugar cannot be directly destroyed in the blood. If you inject even a very small quantity of cane-sugar, dissolved in water, into the blood or under the skin of a rabbit, you find it again in the urine unchanged, with all its chemical

> properties the same. . . . I had soon to give up my first point of view, because this question of the existence of a sugar-producing organ, that I had thought such a hard problem of physiology, was really the first thing revealed to me, as it were of itself, at once."

He kept two dogs on different diets, one with sugar, the other without it; then killed them during digestion, and tested the blood in the hepatic veins:—

> "What was my surprise, when I found a considerable quantity of sugar in the hepatic veins of the dog that had been fed on meat only, and had been kept for eight days without sugar: just as I found it in the other dog that had been fed for the same time on food rich in sugar. . . .
>
> "Finally, after many attempts—*après beaucoup d'essais et plusieurs illusions que je fus obligé de rectifier par des tâtonnements*—I succeeded in showing, that in dogs fed on meat the blood passing through the portal vein does not contain sugar before it reaches the liver; but when it leaves the liver, and comes by the hepatic veins into the inferior vena cava, this same blood contains a considerable quantity of a sugary substance (glucose)."

His further discovery, that this formation of sugar is increased by puncture of the floor of the fourth ventricle, was published in 1849. It is impossible to exaggerate the importance of Claude Bernard's single-handed work in this field of physiology and pathology:—

> "As a mere contribution to the history of sugar within the animal body, as a link in the chain of special problems connected with digestion and nutrition, its value

was very great. Even greater, perhaps, was its effect as a contribution to general views. The view that the animal body, in contrast to the plant, could not construct, could only destroy, was, as we have seen, already being shaken. But evidence, however strong, offered in the form of numerical comparisons between income and output, failed to produce anything like the conviction which was brought home to every one by the demonstration that a substance was actually formed within the animal body, and by the exhibition of the substance so formed.

"No less revolutionary was the demonstration that the liver had other things to do in the animal economy besides secreting bile. This, at one blow, destroyed the then dominant conception that the animal body was to be regarded as a bundle of organs, each with its appropriate function, a conception which did much to narrow inquiry, since when a suitable function had once been assigned to an organ there seemed no need for further investigations. . . .

"No less pregnant of future discoveries was the idea suggested by this newly found-out action of the hepatic tissue, the idea happily formulated by Bernard as 'internal secretion.' No part of physiology is at the present day being more fruitfully studied than that which deals with the changes which the blood undergoes as it sweeps through the several tissues, changes by the careful adaptation of which what we call the health of the body is secured, changes the failure or discordance of which entails disease. The study of these internal secretions constitutes a path of inquiry which has already been trod with conspicuous success, and which promises to lead to untold discoveries of the greatest moment; the gate to this path was opened by Bernard's work." (Sir M. Foster, *loc. cit.*)

V

THE PANCREAS

HERE again Claude Bernard's name must be put first. Before him, the diverse actions of the pancreatic juice had hardly been studied. Vesalius (1543), greatest of all anatomists, makes no mention of the duct of the pancreas, and speaks of the gland itself as though its purpose were just to support the parts in its neighbourhood—*ut ventriculo instar substerniculi ac pulvinaris subjiciatur.* The duct was discovered by Wirsung, about 1640: but anatomy could not see the things that belong to physiology. Lindanus (1653) said, *I cannot doubt that the pancreas expurgates, in the ordinary course of Nature, those impurities of the blood that are too crass and inept to be tamed by the spleen: and, in the extraordinary course, all black bile, begotten of disease or intemperate living.* Wharton (1656) said, *It ministers to the nerves, taking up certain of their superfluities, and remitting them through its duct* *into the intestines.* And Tommaso Bartholini (1666) called it *the biliary vesicle of the spleen.*

This chaos of ideas was brought into some sort of order by Regnier de Graaf, pupil of François de Bois (Sylvius). De Bois had guessed that the pancreas must be considered not according to its position in the body, but according to its structure: that it was analogous to the salivary glands. He urged his pupil to make experiments on it: and de Graaf says—

> "I put my hand to the work: and though many times I despaired of success, yet at last, by the blessing of God on my work and prayers, in the year 1662 I discovered a way of collecting the pancreatic juice."

And, by further experiment, he refuted Bartholini's theory that the pancreas was dependent on the spleen.

Sylvius had supposed that the pancreatic juice was slightly acid, and de Graaf failed to note this mistake; but it was corrected by Bohn's experiments in 1710.

Nearly two hundred years come between Regnier de Graaf and Claude Bernard: it is no wonder that Sir Michael Foster says that de Graaf's work was "very imperfect and fruitless." So late as 1840, there was yet no clear understanding of the action of the pancreas. Physiology could not advance without organic chemistry: de Graaf could no more discover the amylolytic action of the pancreatic juice than Galvani could invent wireless telegraphy. The physiologists had to wait till chemistry was ready to help them :—

> "Of course, while physical and chemical laws were still lost in a chaos of undetermined facts, it was impossible that men should analyse the phenomena of life : first, because these phenomena go back to the laws of chemistry and physics ; and next, because they cannot be studied without the apparatus, instruments, and all other methods of analysis that we owe to the laboratories of the chemists and the physicists." (Cl. Bernard, *Phys. Opér.* p. 61.)

Therefore de Graaf failed, because he got no help from other sciences. But it cannot be called failure ; he must be contrasted with the men of his time, Lindanus and Bartholini, facts against theories, not with men of this century. And Claude Bernard went back to de Graaf's method of the fistula, having to guide him the facts of chemistry observed by Valentin, Tiedemann and Gmelin, and Eberlé. His work began in 1846, and the Académie des Sciences awarded a prize to it in 1850 :—

> "Let this vague conception (the account of the pancreas given in Johannes Müller's Text-book of Physiology) be compared with the knowledge which we at present have of the several distinct actions of the pancreatic juice, and of the predominant importance of this fluid not only in intestinal digestion, but in digestion as a whole, and it will be at once seen what a great advance has taken place in this matter since the early forties. That advance we owe in the main to Bernard. Valentin, it is true, had in 1844 not only inferred that the pancreatic juice had an action

> on starch, but confirmed his view by actual experiment with the juice expressed from the gland; and Eberlé had suggested that the juice had some action on fat; but Bernard at one stroke made clear its threefold action. He showed that it on the one hand emulsified, and on the other hand split up, into fatty acids and glycerine, the neutral fats; he clearly proved that it had a powerful action on starch, converting it into sugar; and lastly, he laid bare its remarkable action on proteid matters." (Sir Michael Foster, *loc. cit.*)

Finally came the discovery that the pancreas—apart from its influences on digestion—contributes its share, like the ductless glands, to the general chemistry of the body:—

> "It was discovered, a few years ago, by von Mering and Minkowski, that if, instead of merely diverting its secretion, the pancreas is bodily removed, the metabolic processes of the organism, and especially the metabolism of carbo-hydrates, are entirely deranged, the result being the production of permanent diabetes. But if even a very small part of the gland is left within the body, the carbo-hydrate metabolism remains unaltered, and there is no diabetes. The small portion of the organ which has been allowed to remain (and which need not even be left in its proper place, but may be transplanted under the skin or elsewhere) is sufficient, by the exchanges which go on between it and the blood generally, to prevent those serious consequences to the composition of the blood, and the general constitution of the body, which result from the complete removal of this organ." (Prof. Schäfer, 1894.)

Here, in this present study of "pancreatic diabetes," by Dr. Vaughan Harley and others, are facts as important as any that Bernard made out: in no way contradicting his work, but added to it. The pancreas is no longer taken to be only a sort of salivary gland out of place: over and above the secretion that it pours into the intestines, it has an "internal secretion," a constituent of the blood: it belongs not only to the digestive system, but also, like the thyroid gland and the supra-renal capsules, to the whole chemistry of the blood and the tissues. So far has physiology come, unaided by anatomy, from the fantastic notions of Lindanus and the men of his time: and has come every inch of the way by the help of experiments on animals.

VI

THE GROWTH OF BONE

THE work of du Hamel proved that the periosteum is one chief agent in the growth of bone. Before him, this great fact of physiology was unknown; for the experiments made by Anthony de Heide (1684), who studied the production of callus in the bones of frogs, were wholly useless, and serve only to show that men in his time knew nothing about the natural growth of bone:—

> "From these experiments it appears—*forsan probatur*—that callus is generated by extravasated blood, whose fluid particles being slowly exhaled, the residue takes the form of the bone: which process may be further advanced by deciduous halitus from the ends of the broken bone."

And Clopton Havers, in his *Osteologia Nova* (London, 1691) goes so far the wrong way that he attributes to the periosteum not the production of bone, but the prevention of over-production; the periosteum is put round the shaft of a bone to compress it, and prevent it from growing too large.

Du Hamel's discovery (1739–1743) came out of a chance observation, made by John Belchier,[1] that the bones of animals fed near dye-works were stained with the dye. Belchier therefore put a bird on food mixed with madder, and found that its bones had taken up the stain. Then du Hamel studied the whole subject by a series of experiments. To estimate the advance that he gave to physiology, contrast de Heide's fanciful language with the title of one of du Hamel's papers—*Quatrième Mémoire sur les Os, dans lequel on se propose de rapporter de nouvelles preuves qui établissent que les os croissent en grosseur par l'addition de couches osseuses qui tirent leur origine du périoste, comme le corps ligneux des Arbres augmente en grosseur par l'aadition de couches ligneuses qui se forment dans l'écorce.* Or take an example of du Hamel's method :—

> "Three pigs were destined to clear up my doubts. The first, six weeks old, was fed for a month on ordinary

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[1] "An Account of the Bones of Animals being changed to a red Colour by Aliment only." By John Belchier, F.R.S., *Phil. Trans. Roy. Soc.*, 1735–36. There is a letter from Sir Hans Sloane, then President of the Royal Society, to M. Geoffroy, member of the French Academy :—"M. Belchier, chirurgien, membre de cette Société, dînant un jour chez un Teinturier qui travaille en Toiles peintes, remarqua que dans un Porc frais qu'on avoit servi sur table, et dont la chair étoit de bon goût, les os étoient rouges. Il demanda la cause d'un effet si singulier, et on lui dit que ces sortes de Teinturiers se servoient de la racine de Rubia Tinctorum, ou garence, pour fixer les couleurs déjà imprimées sur les Toiles de cotton, qu'on appelle en Angleterre callicoes." This passage of dye into the bones of animals had been noted so far back as 1573, by Antoine Mizald, a doctor in Paris—*Erythrodanum, vulgo rubia tinctorum, ossa pecudum rubenti et sandycino colore imbuit.*

food, with an ounce daily of madder-juice—*garence grappe*—put in it. At the end of the month, we stopped the juice, and fed the pig in the ordinary way for six weeks, and then killed it. The marrow of the bones was surrounded by a fairly thick layer of white bone : this was the formation of bone during the first six weeks of life, without madder. This ring of white bone was surrounded by another zone of red bone : this was the formation of bone during the administration of the madder. Finally, this red zone was covered with a fairly thick layer of white bone : this was the layer formed after the madder had been left off. . . . We shall have no further difficulty in understanding whence transudes the osseous juice that was thought necessary for the formation of callus and the filling-up of the wounds of the bones, now we see that it is the periosteum that fills up the wounds, or is made thick round the fractures, and afterward becomes of the consistence of cartilage, and at last acquires the hardness of bones."

These results, confirmed by Bazan (1746) and Boehmer (1751), were far beyond anything that had yet been known about the periosteum. But the growth of bone is a very complex process : the naked eye sees only the grosser changes that come with it ; and du Hamel's ingenious comparison between the periosteum and the bark of trees was too simple to be exact. Therefore his work was opposed by Haller, and by Dethleef, Haller's pupil : and the great authority of Haller's name, and the difficulties lying beyond du Hamel's plain facts, brought about a long period of uncertainty. Bordenave (1756) found reasons for supporting Haller; and Fougeroux (1760) supported du Hamel. Thus men came to study the whole subject with more accuracy —the growth in length, as well as the growth in thickness; the medullary cavity, the development of bone, the nutrition and absorption of bone. Among those who took up the work were Bichat, Hunter, Troja, and Cruveilhier: and they recognised the surgical aspect of these researches in physiology. After them, the periosteal growth of bone became, as it were, a part of the principles of surgery. From this point of view of practice, issued the experiments made by Syme (1837) and Stanley (1849). Finally, with the rise of anæsthetics and of the antiseptic method, came the work of Ollier, of Lyon, whose good influence on the treatment of these cases can hardly be over-estimated.

VII

THE NERVOUS SYSTEM

FROM Galen to the Renaissance, the facts of physiology made no great advance. The authority of Galen, long after the Renaissance, still held good: men forgot his experimental work, and worshipped his name and his doctrines. The ghost or Galen was not laid even by Paracelsus and Vesalius; it haunted our own College of Physicians so late as the middle of the seventeenth century. And this neglect of Galen's method of experiments on animals is well seen in the history of the physiology of the nervous system. Sir Charles Bell took up the experimental study of the nervous system where Galen had left it; you go from the time of Commodus to the time of George the Third, and find Bell putting the finishing touch to Galen's work. It is true that experiments had been made on the nervous system by the men who came before Bell; but they had got overwhelmed with theories. Some of these theories have but lately gone—the nonsense of phrenology, the doctrine that the brain "moves as a whole," the popular belief that its surface is sensitive to touch.[1]

To see how imagination had run riot over the nervous system, take Dr. Risien Russell's list of theories about the cerebellum :—

> "Galen was of opinion that the cerebellum must be the originator of a large amount of vital force. After him, and up to the time of Willis, the prevalent idea seems to have been that it was the seat of memory; while Bourillon considered it the seat of instinct and intelligence. Willis supposed that it presided over involuntary movements and organic functions; and this view, though refuted by Haller, continued in the ascendency for some time. Some believed strongly in its influence on the functions of organic life; and according to some, diseases of the cerebellum appeared to tell on the movements of the heart. . . . Haller believed it to be the seat of sensations, as well as the source of voluntary power; and there were many supporters of the theory that the cerebellum was the seat of the sensory centres. Renzi considered this organ the nervous centre by which we perceive the reality of the external world, and direct and fix our senses on the things round us. Gall, and later Broussais, and others, held that this organ presided over the instinct of reproduction, or the propensity to love; while Carus regarded it as the seat of

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[1] Aristotle, who more than once speaks of experiments on animals, says, "In no animal has the blood any feeling when touched, any more than the excretions; nor has the brain, or the marrow, any feeling when touched." Or we may take Sir Charles Bell's word for it: "I have had my finger deep in the anterior lobes of the brain, when the patient, being at the time acutely sensible, and capable of expressing himself, complained only of the integument." But the fact is so well known that there is no need to quote evidence for it.

the will also. Rolando looked on it as the source of origin of all movements. Jessen adduced arguments in favour of its being the central organ of feeling, or of the soul, and the principal seat of the sensations."

If a better understanding of the nervous system could have been got without experiments on animals, why had men to wait so long for it? The Italian anatomists had long ago given them all the anatomy that could help them. The hospitals, and practice, had given them many hundred years of clinical facts; nervous diseases and head injuries were common enough in the Middle Ages; and by the time of Ambroise Paré, if not before, *post-mortem* examinations were allowed. The one thing wanted was the experimental method; and, for want of it, the physiology of the nervous system stood still. Then, in 1811, came Bell's work. It is most true, that the experimental method is but a part of the science of medicine; that experiment and experience ought to go together like the convexity and the concavity of a curve. But it is true also that men owe their deliverance from ignorance about the nervous system rather to experiments on animals than to any other method of observing facts. Galen showed the way; Bell, Magendie, Marshall Hall, and Claude Bernard, led the way out; and the men who followed them are our leaders now.

1. Sir Charles Bell.

The great authority of Sir Charles Bell has been quoted a thousand times against all experiments on animals :—

> "Experiments have never been the means of discovery ; and a survey of what has been attempted of late years in physiology, will prove that the opening of living animals has done more to perpetuate error than to confirm the just views taken from the study of anatomy and natural motions."

He wrote, of course, in the days before bacteriology, before anæsthetics ; he had in his mind neither inoculations, nor any observations made under chloroform or ether, but just "the opening of living animals." He had also in his mind, and always in it, a great dislike against the school of Magendie. Let all that pass ; our only concern here is to know whether these words are true of his own work.

They occur in a paper, "On the Motions of the Eye, in Illustration of the Uses of the Muscles and Nerves of the Orbit" ; communicated by Sir Humphry Davy to the Royal Society, and read March 20, 1823.[1] This essay was one of a series of papers on the nervous system, presented to the Royal Society during the years 1821–1829. In 1830, having already published four of these papers under the title, "The Exposition of the Nervous System," Bell published all six of them, under the title, "The Nervous System of the Human Body."

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[1] This paper includes an "Experimental Enquiry into the Action of these Muscles," giving an account of an experiment on the eye.

In his Preface to this book (1830) he quotes the earliest of all his printed writings on the nervous system, a pamphlet, printed in 1811, under the title, "An Idea of a New Anatomy of the Brain, Submitted for the Observation of the Author's Friends." We have therefore two statements of his work, one in 1811, the other in 1823 and 1830. The first of them was written when his work was still new before his eyes.

Those who say that experiments did not help Bell in his great discovery—the difference between the anterior and the posterior nerve-roots—appeal to certain passages in the 1830 volume :—

> "In a foreign review of my former papers, the results have been considered as a further proof in favour of experiments. They are, on the contrary, deductions from anatomy ; and I have had recourse to experiments, not to form my own opinions, but to impress them upon others. It must be my apology that my utmost efforts of persuasion were lost, while I urged my statements on the grounds of anatomy alone. I have made few experiments ; they have been simple and easily performed, and I hope are decisive. . . .
>
> "My conceptions of this matter arose by inference from the anatomical structure ; so that the few experiments which have been made were directed only to the verification of the fundamental principles on which the system is established."

If it were not for the 1811 pamphlet, the opponents of all experiments on animals might claim Sir Charles

Bell on their side. But while his work was still a new thing, he spoke in another way of it :—

> "I found that injury done to the anterior portion of the spinal marrow convulsed the animal more certainly than injury to the posterior portion ; but I found it difficult to make the experiment without injuring both portions.
>
> "Next, considering that the spinal nerves have a double root, and being of opinion that the properties of the nerves are derived from their connexions with the parts of the brain, *I thought that I had an opportunity of putting my opinion to the test of experiment, and of proving at the same time* that nerves of different endowments were in the same cord (nerve-trunk) and held together by the same sheath.
>
> "On laying bare the roots of the spinal nerves, I found that I could cut across the posterior fasciculus of nerves, which took its origin from the posterior portion of the spinal marrow, without convulsing the muscles of the back ; but that on touching the anterior fasciculus with the point of the knife, the muscles of the back were immediately convulsed.
>
> "*Such were my reasons for concluding* that the cerebrum and cerebellum were parts distinct in function, and that every nerve possessing a double function obtained that by having a double root. *I now saw the meaning* of the double connexion of the nerves with the spinal marrow ; and also the cause of that seeming intricacy in the connexions of nerves throughout their course, which were not double at their origins."

It is impossible to reconcile the 1830 sentences with this vivid personal account of himself; *I had an oppor-*

tunity of putting my opinion to the test of experiment . . . an opportunity of proving. . . . Such were my reasons for concluding. . . . I now saw. . . . It is just what all men of science say of their experiments : the very phrase of Archimedes, and Asellius, and de Graaf. If Sir Charles Bell had been working at the facts of chemistry or of botany, who would have doubted the meaning of these words ?

This same inconsistency of sentences occurs elsewhere in his "Nervous System of the Human Body." In one place he says that he has made few experiments : *They have been simple, and easily performed, and I hope are decisive.* In another he says, "*After making several experiments on the cerebrum and cerebellum, I laid the question of their functions entirely aside*, and confined myself to the investigation of the spinal marrow and the nerves ; *a subject which I found more within my power*, and which forms the substance of the present volume."

Or take his account of the cranial nerves :—

> "It was necessary to know, in the first place, whether the phenomena exhibited on injuring the separate roots corresponded with what was suggested by their anatomy. . . .
>
> "Here a difficulty arose. An opinion prevailed that ganglions were intended to cut off sensation ; and every one of these nerves, which I supposed were the instruments of sensation, have ganglions on their roots. Some very decided experiment was necessary to overturn this dogma. (Account of the experiment.) By pursuing the

inquiry, it was found that a ganglionic nerve is the sole organ of sensation in the head and face : ganglions were therefore no hindrance to sensation ; and thus my opinion was confirmed. . . . *It now became obvious* why the third, sixth, and ninth nerves of the encephalon were single nerves in their roots. . . .

"Observing that there was a portion of the fifth nerve which did not enter the ganglion of that nerve, and being assured of the fact by the concurring testimony or anatomists, I conceived that the fifth nerve was in fact the uppermost nerve of the spine. . . . This opinion was confirmed by experiment. . . . (Account of an experiment on the dead body). On dividing the root of the nerve in a living animal, the jaw fell relaxed. Thus its functions are no longer matter of doubt : it is at once a muscular nerve and a nerve of sensibility. And thus the opinion is confirmed, that the fifth nerve is to the head, what the spinal nerves are to the other parts of the body, in respect to sensation and volition."

The value of the experimental method could hardly be stated in more emphatic words. He supposed something, conceived it, had an opinion about it. Anatomy had suggested something to him. He put his opinion to the test of phenomena, that is to say, to the test of visible facts ; and then his opinion was confirmed. As with the spinal nerve-roots, so with the fifth cranial nerve—his work was successful, because he followed the way of experiment.

He was by nature of a most complex and sensitive temperament, full of contrary forces, one man in 1811, another in 1830. In 1811 he wrote, *I now saw the* *meaning of the double connexion of the nerves*; in 1830 he had come to hate the *stupid sterile materialism* of the French school: he beheld anatomy falling behind physiology, and his Windmill Street school perishing to make way for the Hospital schools and for the University of London. He was before everything else a great anatomist: he stood up for the honour of anatomy against the new physiology, and for the honour of the Monroes and the Hunters against Magendie: he hated the notion that any man should proceed to experiments on function till the very last secrets had been got out of structure. He died a few years afterward. The 1830 writings are his last stand for the defence of his country, his school, and his beloved anatomy, against the methods of Magendie; who said of himself, "I am a mere street scavenger, *chiffonier*, of science. With my hook in my hand and my basket on my back, I go about the streets of science, collecting what I find."

This open conflict between Bell's first and last thoughts is a part of his character: he was brilliant, impulsive, changeable, inconsistent; and, what is more important, his honour kept him from trying to evade this trumpery charge of inconsistency; and he reprinted the 1811 Preface in the book that he published in 1830. Doubtless he would have picked his words more carefully if he had foreseen that one of the 1830 sentences would be wrested out of its place in his life's work, and used as false evidence against the very method that he followed.[1]

His observations on the cranial nerves brought about an immediate change in the practice of surgery :—

> "Up to the time that Sir Charles Bell made his experiments on the nerves of the face, it was the common custom of surgeons to divide the facial nerve for the relief of neuralgia, *tic douleureux;* whereas it exercises, and was proved by Sir Charles Bell to exercise, no influence over sensation, and its division consequently for the relief of pain was a useless operation." (Sir J. Erichsen.)

2. Marshall Hall.

Reflex action had been studied long before the time of Marshall Hall. Sir Robert Boyle (1663) had observed the movements and actions of decapitated vipers, flies, silkworms, and butterflies. Similar observations were made on frogs, eels, and other lower animals, by Redi, Woodward, Stuart, Le Gallois, and Sir Gilbert Blane. According to Richet, it was Willis who first gave the name *reflex* to these movements.

It cannot be said that these first studies of reflex action did much for physiology. But the following translation from Prochaska (1800) shows how they cleared the way for Marshall Hall's work, by the proof that they gave of the liberation of nervous energy in the spinal cord :—

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[1] The relation of Magendie's work on the nerve-roots to Bell's work need not be considered here. The exact dates of Bell's observations are given by one of his pupils in the Preface to the 1830 volume. Magendie finally proved the sensory nature of the posterior nerve-roots : "The exact and full proof which he brought forward of the truth which Charles Bell had divined rather than demonstrated, that the anterior and posterior roots of spinal nerves have essentially different functions—a truth which is the very foundation of the physiology of the nervous system—is enough by itself to mark him as a great physiologist." (Sir M. Foster, *loc. cit.*)

> "These movements of animals after decapitation must needs be by consent and commerce betwixt the spinal nerves. For a decapitated frog, if it be pricked, not only draws away the part that is pricked, but also creeps and jumps ; which cannot happen but by consent betwixt the sensory nerves and the motor nerves. The seat of which consent must needs be in the spinal cord, the only remaining portion of the sensorium. *And this reflexion of sensory impressions into motor impressions is not accomplished in obedience to physical laws alone—wherein the angle of reflexion is equal to the angle of incidence, and reaction to action—but it follows special laws as it were written by Nature on the spinal cord, which we can know only by their effects, but cannot fathom with the understanding.* But the general law, whereby the sensorium reflects sensory impressions into motor impressions, is the preservation of ourselves."

It was not possible, in 1800, to go further, or to put the facts of reflex action more clearly: but this fine sentence gives no hint of the truth that guided Marshall Hall—that the "consent and commerce" of reflex action are to be found at definite points or levels in the spinal cord ; that the cord no more "works as a whole" than the brain. The greatness of Marshall Hall's work lies in his recognition of the divisional action of the cord: he proved the existence of definite centres in it, he discovered the facts of spinal localisation, and thus foreshadowed the discovery of cerebral localisation. In his earlier writings (1832–33) he showed how the movements of the trunk and of the limbs are only one sort of reflex action; how the larynx, the pharynx, and the sphincter muscles, all act by the "consent and commerce" of the spinal cord. Later, in 1837, he demonstrated the course of nerve-impulses along the cord from one level to another, the results of direct stimulation of the cord, and other facts of spinal localisation. He noted the different effects of opium and of strychnine on reflex action; and he extended the doctrines of reflex action beyond physiology to the convulsive movements of the body in certain diseases.[1]

3. Flourens.

Beside his work on the nervous system, Flourens (1794–1867) studied the periosteal growth of bone, and the action of chloroform;[2] but he is best known by his experiments on the respiratory centre and the cerebellum. The men who interpreted the nervous system followed the anatomical course of that system: first the nerve-roots, then the cord, then the medulla oblongata and the cerebellum, and last the cerebral hemispheres; a steady upward advance, from the observation of decapitated insects to the localisation of centres in the human brain. Flourens, by his work on the medulla oblongata, localised the respiratory centre, the nerve-cells for the reflex movements of respiration:—

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[1] Contrast with Marshall Hall's writings a sentence quoted in Bryan's *Antivivisection Evidences* (1895): "No experiments at all are needed for demonstrating the processes of reflex action."

[2] When Flourens died, Claude Bernard was appointed to his place in the French Academy; and, in the *Discours de Reception* (May 27, 1869), said, "It is twenty-two years since the discovery of anæsthesia by ether came to us from the New World, and spread rapidly over Europe. M. Flourens was the first man who showed that chloroform is more active than ether."

> "M. Flourens a circonscrit ce centre avec une scrupuleuse précision, et lui a donné le nom de *nœud vital*." (Cl. Bernard.)

Afterward came the discovery of cardiac and other centres in the same portion of the nervous system. Flourens also showed that the cerebellum is concerned with the equilibration of the body, and with the co-ordination of muscular movements; that an animal, a few days old, deprived of sensation and consciousness by removal of the cerebral hemispheres, was yet able to stand and move forward, but, when the cerebellum was removed, its muscles lost all co-ordinate action. (*Recherches Expérimentales*, Paris, 1842.) And from his work, and the work of those who followed him, on the semicircular canals of the internal ear, came the evidence that these minute structures are the terminal organs of equilibration: that as the special senses have their terminal apparatus and their central apparatus, so the semicircular canals and the cerebellum are the terminal and central apparatus for the sense of equilibrium.

4. Claude Bernard.

The discovery of the vaso-motor nerves, and of the control of the nervous system over the calibre of the arteries, was made by Claude Bernard at the outset of his work on the influence of the nervous system on the temperature.[1] The evidence of Professor Sharpey before the Royal Commission of 1875 shows how things had been misjudged, before Bernard's time, in the light of *views taken from the Study of Anatomy and Natural Motions*:—

> "I remember that Sir Charles Bell gave the increased size of the vessels in blushing, and their fulness of blood, as an example of the increased action of the arteries in driving on the blood. It turns out to be just the reverse, inasmuch as it is owing to a paralysis of the nerves governing the muscular coats of the arteries."

Claude Bernard's first account of his work was communicated to the Société de Biologie in December, 1851. The following description is taken from his *Leçons de Physiologie Opératoire*:—

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[1] A full account of this discovery, and of its relation to the experiments of Brown Séquard, Waller, and Budge, is given by Sir Michael Foster in his Life of Claude Bernard; and the question of priority between Bernard and Brown Séquard need not be considered here, for the experimental method was the only way open to either of them.

"I will remind you how I was led to the discovery of the vaso-motor nerves. Starting from the clinical observation, made long ago, that in paralysed limbs you find at one time an increase of cold, and at another an increase of heat, I thought this contradiction might be explained by supposing that, side by side with the general action of the nervous system, the sympathetic nerve might have the function of presiding over the production of heat; that is to say, that in the case where the paralysed limb was chilled, I supposed the sympathetic nerve to be paralysed, as well as the motor nerves; while in the paralysed limbs that were not chilled the sympathetic nerve had retained its function, the systemic nerves alone having been attacked.

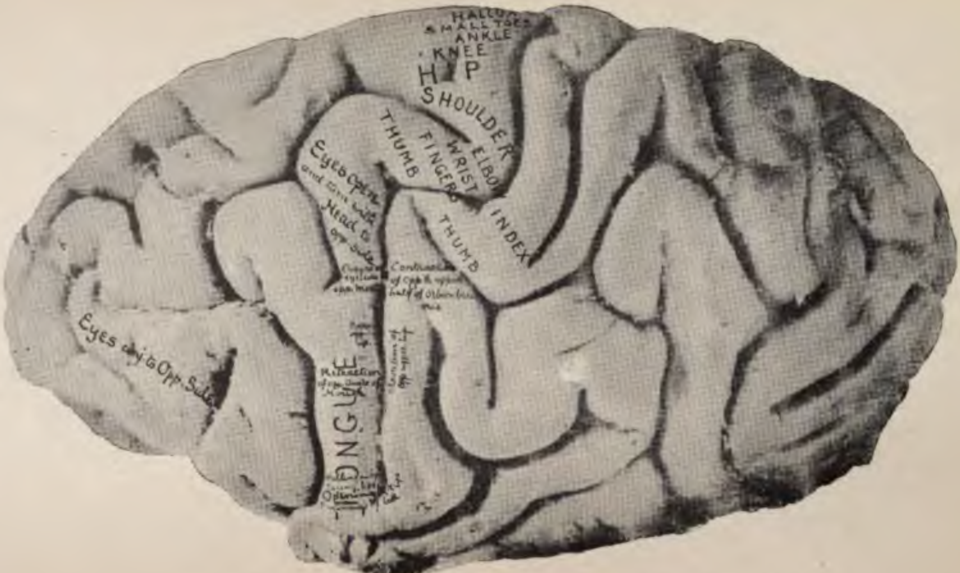
"This was a theory, that is to say, an idea leading me to make experiments; and for these experiments I must find a sympathetic nerve-trunk of sufficient size, going to some organ that was easy to observe, and must divide this trunk to see what would happen to the heat-supply of the organ. You know that the rabbit's ear, and the cervical sympathetic nerve of this animal, offered us the required conditions. So I divided the nerve; and immediately my experiment gave the lie direct to my theory—*Je coupai donc ce filet et aussitôt l'expérience donna à mon hypothèse le plus éclatant démenti.* I had thought that the section of the nerve would suppress the function of nutrition, of calorification, over which the sympathetic system had been supposed to preside, and would cause the hollow of the ear to become chilled; and here was just the opposite, a very warm ear, with great dilatation of its vessels.

"I need not remind you how I made haste to abandon my first theory, and gave myself to the study of this new state of things. And you know that here was the starting-point of all my researches into the vaso-motor and thermic system; and the study of this subject is become one of the richest fields of experimental physiology."

Waller, in 1853, studied the vaso-motor centre in the spinal cord; and Schiff, in 1856, found evidence of the existence of two kinds of vaso-motor nerves—those that constrict the vessels and those that dilate them. This view was finally established in 1858 by Claude Bernard's experiments on the chorda tympani and the submaxillary gland.

The *Leçons de Physiologie Opératoire* were published in 1879. Twenty years later, Sir Michael Foster says of Bernard's work—

"It is almost impossible to exaggerate the importance of these labours of Bernard on the vaso-motor nerves, since it is almost impossible to exaggerate the influence which our knowledge of the vaso-motor system, springing as it does from Bernard's researches as from its fount and origin, has exerted, is exerting, and in widening measure will continue to exert, on all our physiological and pathological conceptions, on medical practice, and on the conduct of human life. There is hardly a physiological discussion of any width in which we do not sooner or later come on vaso-motor questions. Whatever part of physiology we touch, be it the work done by a muscle, be it the various kinds of secretive labour, be it the insurance of the brain's well-being in the midst of the hydrostatic vicissitudes to which the changes of daily life subject it, be it that maintenance of bodily temperature which is a condition of the body's activity; in all these, as in many other things, we find vaso-motor factors intervening. And if, passing


HALLUX
SMALL TOES
ANKLE
KNEE
HIP
SHOULDER
ELBOW
WRIST
FINGERS
THUMB
INDEX
THUMB
Eyes open and turn with Head to opp. side
Contraction of opp. & upper half of Orbicularis
TONGUE
Retraction of opp. angle of Mouth
Opening
Eyes to Opp. Side

Brain of a Monkey, with Motor Centres marked on it.

(From Dr. C. E. Beevor's work on "The Diseases of the Nervous System.")

the insecure and wavering line which parts health from illness, we find ourselves dealing with inflammation, or with fever, or with any of the disordered physiological processes which constitute disease, we shall find, whatever be the tissue specially affected by the morbid conditions, that vaso-motor influences have to be taken into account. The idea of vaso-motor action is woven as a dominant thread into all the physiological and pathological doctrines of to-day; attempt to draw out that thread, and all that would be left would appear as a tangled heap."

5. Cerebral Localisation.

Finally, moving upward along the anatomy of the nervous system, physiology came to study the motor centres and special-sense centres of the cerebral hemispheres. And it is one of many instances how science and practice work together, that the study of these centres began not in experiment but in experience. The first fact of cerebral localisation came out of Bouillard's series of cases (1825); then Dax (1836), then Broca (1861). Clinical observation and *post-mortem* examination found the speech-centres; physiological experiments had nothing to do with it. But at once, so soon as practice gave the word to science, physiology set to work. These clinical facts had been there all the time; loss of speech had gone with disease or injury of "Broca's convolution" ever since man had been on the earth, and nobody had observed and recorded the sequence. Then, after 1861, everything was changed, and in a few years physiology had mapped out a large part of the surface of the brain, had discovered its departmental work, divided and subdivided its convolutions, and charted and settled once and for ever the amazing geography of the motor centres. There is nothing more wonderful in the whole kingdom of science.

The story of Broca's convolution is told in Hamilton's Text-book of Pathology :—

> "In 1825, Bouillard collected a series of cases to show that the faculty of speech resided in the frontal lobes. In the year 1836 M. Dax, in a paper read to the Medical Congress of Montpellier, stated as a result of his researches that, where speech was lost from cerebral causes, he believed the lesion was invariably found in the left cerebral hemisphere, and that the accompanying paralysis of the right side of the body is consequent upon this. This paper for long lay buried in the annals of medical literature, but was unearthed years afterwards by his son, and presented to the French Academy. Bouillard's views were also disinterred by Aubertin, and in the year 1861 were brought by him before the notice of the Anthropological Society of Paris. Broca, who was present at the meeting, had a patient under his care at the time who had been aphasic (without power of speech) for twenty-one years, and who was in an almost moribund state. The autopsy proved of great interest, as it was found that the lesion was confined to the left side of the brain, and to what we now call the third frontal convolution. Broca was struck with the coincidence; and when a similar case came under his care afterwards, unaware of what had been done by Dax, he postulated the conclusion that the integrity of the third frontal convolution, and perhaps also

part of the second, is essential to speech. In a subsequent series of fifteen typical cases examined, it was found that the lesion had destroyed, among other parts, the posterior part of the third frontal in fourteen. In the fifteenth case the destruction had taken place in the island of Reil and temporal lobe."

After 1861 physiology took the lead, and kept it. But, through all the work, science and practice have kept touch together: and there is nothing more splendid in the whole history of their co-operation than this triumphant mapping-out of the surface of man's brain. No need to put here the names of the men who did it, for they are household words, the names of the very elect in the science and art of medicine and surgery.

These instances are but a part of the results gained by experiments in physiology. Nothing has been said of the work of Boyle, Hunter, Lavoisier, Haldane, Despretz, and Regnault, on animal heat and respiration; of Petit, Dupuy, Breschet, and Reid, on the sympathetic system; of Galvani, Volta, Haller, du Bois-Reymond, and Pflüger, on muscular contractility. And, for good reasons, more has been said of the past than of the present. First, because it was necessary to put an end to the false statements that are made, by those who are opposed to all experiments on animals, about the work done in the past. Next, because physiology, in the present, is wrought to finer issues, that are not all intelligible for general reading. Next, because it is impossible now to isolate physiology; to say, for example, that the study of the internal secretions, or of natural immunity, or of the interdependence in action of organs that are independent in structure, belongs to physiology alone, not also to pathology. For it is impossible to have back the simpler problems of the past, to discover the circulation of the blood twice, "as though a miracle could be encored." But the experimental method, alike in the past and in the present, has been the chief way of advance; as Mr. Darwin said, in his evidence before the Royal Commission of 1875: "I am fully convinced that physiology can progress only by the aid of experiments on living animals. I cannot think of any one step which has been made in physiology without that aid."

EXPERIMENTS IN PATHOLOGY, BACTERIOLOGY, AND THERAPEUTICS

I

INFLAMMATION

PATHOLOGY is a younger science than physiology, because the use of the microscope was the beginning of pathology: and the microscope, only sixty years ago, was very different from the microscope to-day. The great pathologists of that time had not the lenses, microtomes, and staining-fluids of their successors. And now, within the world of pathology, the New World of bacteriology has been found. Go back only twenty-five years, to the date of the Royal Commission on experiments on animals, 1875: read the evidence of the witnesses, how little is said about pathology, and of bacteriology hardly a word. They "believe they are beginning to get an idea of the nature of tubercle." Take what Sir John Simon says, in his evidence, about anthrax—a magnificent prophecy, that yet failed to influence the authorities who drafted the Act:—

> "We are going through a progressive work that has many stages, and are now getting more precise knowledge of the contagium. By these experiments on sheep it has been made quite clear that the contagium of sheep-pox (anthrax) is *something of which the habits can be studied, as the habits of a fern or a moss can be studied: and we look forward to opportunities of thus studying the contagium outside the body which it infects. This is not a thing to be done in a day, nor perhaps in ten years, but must extend over a long period of time.* Dr. Klein's present paper represents one very important stage of a vast special study. He gives the identification of the contagium as *something which he has studied to the end in the infected body, and which can now in a future stage be studied outside the body.*"

Or take Koch's first account of the tubercle-bacillus, March 24, 1882—less than eighteen years ago:—

> "Henceforth, in our warfare against this fearful scourge of our race, we have to reckon *not with a nameless something, but with a definite parasite, whose conditions of life are for the most part already known, and can be further studied. . . . Before all things, we must shut off the sources of the infection*, so far as it is in the power of man to do this."[1]

These conditions of life have been studied, in all species of bacteria, with amazing accuracy. It has been proved, past possibility of doubt, that the pathogenic bacteria are the cause of infective diseases; they have fulfilled Koch's postulates—that they should be found in the diseased tissues, be cultivated outside the body, reproduce the same disease in animals, and be found again in the tissues of those animals. By an immeasurable amount of hard work crowded into a few years, this newer world of bacteriology has been entered and subdued. The Commissioners of 1875, speaking of physiological experiments only, said, "It would require a voluminous treatise to exhibit in a consecutive statement the benefits that medicine and surgery have derived from these discoveries." If physiology in 1875 required a treatise, bacteriology in 1900 will want a shelf.

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[1] "In Zukunft wird man es im Kampf gegen diese schreckliche Plage des Menschengeschlechtes nicht mehr mit einem unbestimmten Etwas, sondern mit einem fassbaren Parasiten zu thun haben, dessen Lebensbedingungen zum grössten Theil bekannt sind und noch weiter erforscht werden. Es müssen vor allen Dingen die Quellen, aus denen der Infections-stoff fliesst, so weit es in menschlichen Macht liegt, verschlossen werden."

But the advance of modern pathology is not all due to bacteriology. Take, for example, inflammation. Long before bacteria came to be studied, every other fact of inflammation had been watched under the microscope: the most minute changes in the affected tissues, the slowing and arrest of the blood in the capillaries, and the escape of blood-cells out of the capillaries into the tissues. Everything had been made ready for the fuller interpretation that was coming from bacteriology: the old naked-eye descriptions of inflammation were left behind: men set aside the definition of Celsus, that it was *rubor et tumor cum calore et dolore*—words that sound like Molière's jest about the *vis dormitiva* of opium—they watched inflammation under the microscope, in such transparent structures as the frog's web and mesentery, the bat's wing, and the tadpole's tail. It was thus that Wharton Jones observed the rhythmical contraction of the veins in the bat's wing. The discovery of the escape of the leucocytes (white blood-cells) was made by Waller and Cohnheim.

To those who are opposed to all experiments on animals it may seem a small thing that a blood-cell should be on one side or the other of a microscopic film in a tadpole's tail. But this migration of amœboid cells from the capillaries into the tissues, the first move of the blood in the fight against disease, is now seen in the light of Metchnikoff's work as a fact of the utmost importance. And the whole doctrine of inflammation goes back to the observation, under the microscope, of living tissues inflamed by the scratch of a needle or the touch of an acid.

II

SUPPURATION AND "BLOOD-POISONING"

ALL suppuration, and all forms of "blood-poisoning"—abscesses, boils, carbuncles, erysipelas, puerperal fever, septicæmia, pyæmia—are due to minute organisms, various kinds of *micrococcus*. It has indeed been shown that suppuration may, in exceptional conditions, occur without micro-organisms: but practically every case of suppuration is a case of infection either from without or from within the body. There is no room here for any account of the work spent on these micrococci: on their identification, isolation, culture, and inoculation. It is the same with all the pathogenic bacteria—each kind has its own habits, phases, and idiosyncrasies, antagonisms, and preferences: nothing is left unstudied—the influences of air, light, heat, and chemistry; all the facts of their growth, division, range of variation, grades of virulence, vitality, and products; the entire life and death of each species, and everything that it is, and does, and can be made to do:—

> "Doubtless immense progress has been made during the last two or three decades, but a vast amount still remains to be done. We have only touched the fringe of the explanation of the difficult problems of immunity, of the extraordinary variations in virulence and effects of the same organism, and of the important question of cure in, and prevention of, infective diseases; while the chemistry of the products of bacterial activity is but in its infancy." (Hewlett, *Manual of Bacteriology*, 1898.)

The difficulties of bacteriology are written across every page of the text-books: above all, the difficulties of attenuating or intensifying the virulence of bacteria, and of immunising animals, and of procuring from them an immunising serum of exact and constant strength. Every antitoxin is the outcome of an immeasurable expenditure of hard international work, unsurpassed in all science for the fineness of its methods and the closeness of its arguments.

But the *Zoophilist* (March, 1898) has a ready explanation for all the problems of bacteriology:—

> "We are often asked if there is any germ of truth at all in the serum treatment of disease. There is; and it is as well that our readers should know exactly what it is. In infectious diseases, a proportion of the delicate blood-corpuscles die and become waste matter in the blood. If the patient be of good constitution, his system soon eliminates this dead matter. Now all serums being very

liable to decomposition are preserved by a small proportion of carbolic acid, and this being injected hypodermically acts antiseptically in the blood, and so assists nature in getting rid of the decomposing corpuscles."[1]

The older theories of disease had attributed infection to the intemperature of the weather, the powers of the air, or the work of the devil: later, men recognised that there must be a *materies morbi*, something particulate, perhaps something alive; but it was still "a nameless something": they overestimated the constitutional, personal aspect of a case of infective disease, against the facts of local infection or inoculation with a specific organism, and studied with infinite care everything but the real cause of the trouble. Read the life of Semelweiss; or the story told of Pasteur by M. Roux, in his *L'Œuvre Médicale de Pasteur* (*Agenda du Chimiste*, 1896, p. 528):—

"Dans le pus des abcès chauds et dans celui des furoncles on constate un petit organisme arrondi, disposé en amas qu'on cultive facilement dans le bouillon. On le retrouve dans l'osteomyélite infectieuse des enfants. Pasteur affirme que l'ostéomyélite et le furoncle sont deux formes d'une même maladie, et que l'ostéomyélite est le furoncle de l'os. En 1878, cette assertion a fait rire bien les chirurgiens.

"Dans les infections puerpérales, les caillots renferment un microbe à grains arrondis se disposant en files. Cet aspect en chapelet est surtout manifesté dans les cultures. Pasteur n'hésite pas à déclarer que cet organisme microscopique est la cause la plus fréquente des infections chez les femmes accouchées. Un jour, dans une discussion sur la fièvre puerpérale à l'Académie de médecine, un de ses collégues le plus écoutés dissertait éloquemment sur les causes des épidémies dans les maternités. Pasteur l'interrompt de sa place : 'Ce qui cause l'épidémie, ce n'est rien de tout cela : c'est le médecin et son personnel qui transportent le microbe d'une femme malade à une femme saine.' Et comme l'orateur répondit qu'il craignait fort qu'on ne trouve jamais ce microbe, Pasteur s'élance vers le tableau noir, dessine l'organisme en chapelet de grains en disant : 'Tenez, voici sa figure."

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[1] As Ambroise Paré said of the spells and magic of his time, *It is pleasant to know this way of practising medicine.* But the *Zoophilist* can appeal to one American journal, with a medical title, to support this amazing method of "assisting Nature."

That is the note of modern pathology—*Tenez, voici sa figure*. Contrast the older teaching about erysipelas, typhoid fever, or tetanus, with the present knowledge that men have of these infective diseases: go back only twenty years, and you are in another world.

And, of course, pathology and surgery have advanced together. The antiseptic method was based on bacteriology, resting as it did on the proof afforded by Pasteur that putrefaction was caused by bacteria, and not by the oxygen of the air as had been previously believed.

And the study of the micrococci has not only proved and made perfect the present methods of surgery; it has also discovered a serum for the treatment of cases of micrococcic infection. Take, for example, the disease called ulcerative endocarditis, the growth of micrococci on the valves of the heart, whence they are carried by the blood into different parts of the body. Several cases have lately been reported, where recovery from this most hopeless disease has followed the use of the antistreptococcic serum.[1] It has also given excellent results in cases of puerperal fever, and in cases of dissection wounds. Already, though it is a new thing, it has saved many lives, and is steadily gaining ground in practice. It has also been used, to avert the risk of infection, before certain operations where the antiseptic method cannot be strictly enforced.

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[1] See, among these, two of special interest: *Lancet*, January 21 and February 11, 1899; and the recent debate at the annual meeting of the British Medical Association at Portsmouth, August, 1899.

III

ANTHRAX

IN animals, anthrax is also called *charbon*, splenic fever, or splenic apoplexy.[1] In man, the name of *malignant pustule* is given to the sloughing sore at the point of accidental inoculation; and the name of *wool-sorters' disease* is given to those cases of anthrax where the lungs are affected by inhalation of the spores of the bacillus. Anthrax occurs mostly among butchers, hide-dressers, wool-sorters, and rag-pickers: among animals, in sheep, cattle, horses, and swine.[2] Wool-sorters' disease was first noticed in the Bradford worsted district after the introduction of alpaca and mohair as textile materials in 1837.

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[1] The Board of Agriculture has lately issued a new Anthrax Order (1899), enforcing early notification, examination of suspected animals, deep burial of carcasses in quicklime, &c. The skin of the carcass must not be cut, its nostrils must be plugged, &c. "Formerly, farmers believed that anthrax was the result of feeding cattle upon too highly nutritious or artificial foods, and that death was the result of apoplexy. It would be well if farmers, and the public generally, took the proper view of the illness." (*British Medical Journal*, February 4, 1899.)

[2] "Many of the outbreaks of anthrax in this country have been in the neighbourhood of Bradford, and have been traced to the use of infected wool-refuse as manure. A map published by the Board of Agriculture shows that the outbreaks of anthrax are most frequent in those counties of Great Britain where dry foreign wools, hairs, hides, and skins are manufactured into goods. In 1892 there were forty-two outbreaks of

The bacillus anthracis was first seen no less than fifty years ago. Pollender in 1844, Roger and Davaine in 1850, noted the *petits bâtonnets* in the blood of sheep dead of the disease, and thought they were some sort of microscopic blood-crystals: it was not till 1863, after Pasteur's study of lactic-acid fermentation, that Davaine realised they were living organisms. Afterward, Koch succeeded in making cultures of them, and reproduced the disease by inoculating animals with these cultures; yet it was said, so late as 1876, that the bacillus anthracis was not the cause of anthrax, but only the sign of it: "Along with the bacilli, there are blood cells and blood-plasma, and these contain the true amorphous virus of anthrax." Then came Pasteur's work, and reached its end in the experiments at Chartres, and the famous test-inoculations (1881) at Pouilly-le-Fort.

In the *Agenda du Chimiste* (1896) M. Roux gives the following account of this work, which he had watched from first to last:—

"Vaccination against *charbon* has now been put to the test of practice for fourteen years. Wherever it is adopted, there

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anthrax in the West Riding of Yorkshire, as against two in the North Riding and one in the East Riding. . . . An undoubted fact in connection with anthrax is its tendency to recur on certain farms. During 1895, the disease reappeared on 23 farms or other premises in England, and 6 in Scotland, where it had been reported in the previous year." (Dr. Poore's Milroy Lectures, *On the Earth in relation to Contagia*, 1899.)

the losses from *charbon* have become insignificant. It was followed by vaccination against swine-measles, *rouget des porcs*, the special study of our poor friend Thuillier.[1] But the immediate result of Pasteur's vaccinations is their least merit: they have given men absolute faith in a science that could show such good works, they have started a movement that is irresistible; above all, they have set going the whole study of immunity, which is bringing us at last to a right way of treating infective diseases.

"Virulence is a quality that microbes can lose; or they can acquire it. Suppose we came across the anthrax-bacillus so far attenuated, in the way of Nature, that it had lost all power to kill—of course we should fail to recognise it; we should take it for an ordinary bacillus of putrefaction: you must watch it through each phase of its attenuation, to know that the harmless organism is the descendant of the fatal virus. But you can give back to it the virulence that it has lost, if you put it, to begin with, under the skin of a very delicate subject, a mouse only one day old. With the blood of this mouse inoculate another, a little older, and it will die. Passing by this method from younger to older mice, we come to kill adult mice, guinea-pigs, then rabbits, then sheep, &c. Thus, by transmission, the virus gains strength as it goes. Doubtless this increase of virulence, that we bring about by experiment, occurs also in Nature; and it is easy to see how a microbe, usually harmless to this or that species of animals, might become deadly to it. Is not this the way that infective diseases have appeared on the earth from age to age?

"*See how far we have come, from the old metaphysical ideas about virulence, to these microbes that we can turn this way*

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[1] M. Thuillier was a member of the French Cholera Commission (Egypt, 1883), and died of cholera at his work.

or that way—stuff so plastic that a man can work on it, and fashion it as he likes."

Pasteur's note on the attenuation of anthrax was presented to the Académie des Sciences on February 28, 1881; and the test-inoculations at Pouilly-le-Fort were made in May of that year. It was hardly to be expected that every country, in every year, should obtain such results as France now takes as a matter of course; and at one time, about sixteen years ago, there was in Hungary a "conscientious objection" to the inoculation of herds against the disease.[1] In Italy last year, from May 1, 1897, to April 30, 1898, the issue of anticharbon vaccine from one institute alone, the Sero-Therapeutic Institute at Milan, was 165,000 tubes, enough to inoculate 33,734 cattle and 98,792 sheep. And in France, between 1882 and 1893, more than three million sheep, and nearly half a million cattle, were inoculated.

The work done in France was published by M. Chamberland, in the *Annales de L'Institut Pasteur*, March, 1894. The following translation of his memoir—*Résultats pratiques des Vaccinations contre le Charbon et le Rouget en France*—shows something of the national influence of the Pasteur Institute :—

1. CHARBON.

After the famous experiments at Pouilly-le-Fort,

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[1] The initial failures, here and there, in 1882–84, are still paraded as evidence against experiments on animals. See the *Zoophilist*, February and July, 1893, and Bryan, *Antivivisection Evidences*, 1895.

MM. Pasteur and Roux entrusted to me the whole method and practice of the vaccinations against *charbon*. Twelve years have passed, and it is now time to put together the results, and to make a final estimate of the value of these preventive inoculations.

Every year, we ask the veterinary surgeons to report

1. The number of animals they have vaccinated.
2. The number that have died after the first vaccination.
3. The number that have died after the second vaccination, within the twelve days following it.
4. The number that have died during the rest of the year.
5. The average annual mortality before the practice of vaccination.

The sum total of all the reports is given in the tables. (See opposite page.)

Comparing the figures in the fourth column with those in the second, we see that a certain number or veterinary surgeons neglect to send their reports at the end of the year. The number of reports that come to us even tends to get less each year. The fact is that many veterinary surgeons who do vaccinations every year content themselves with writing, 'The results are always very good ; it is useless to send you reports that are always the same.'

We have every reason to believe, as a matter of fact, that those who send no reports are satisfied ; for if any-

ANTHRAX

VACCINATION AGAINST CHARBON (FRANCE)

Sheep.

Years.	Total number of animals vaccinated.	Number of Reports.	Animals vaccinated according to reports received.	Mortality.			Total.	Total loss per 100.	Average loss before vaccination
				After first vaccination.	After second vaccination.	During the rest of the year.			
1882	270,040	112	243,199	756	847	1,037	2,640	1·08	10%
1883	268,505	103	193,119	436	272	784	1,492	0·77	,,
1884	316,553	109	231,693	770	444	1,033	2,247	0·97	,,
1885	342,040	144	280,107	884	735	990	2,609	0·93	,,
1886	313,288	88	202,064	652	303	514	1,469	0·72	,,
1887	293,572	107	187,811	718	737	968	2,423	1·29	,,
1888	269,574	50	101,834	149	181	300	630	0·62	,,
1889	239,974	43	88,483	238	285	501	1,024	1·16	,,
1890	223,611	69	69,865	331	261	244	836	1·20	,,
1891	218,629	65	53,640	181	102	77	360	0·67	,,
1892	259,696	70	63,125	319	183	126	628	0·99	,,
1893	281,333	30	73,939	234	56	224	514	0·69	,,
Total	3,296,815	990	1,788,879	5,668	4,406	6,798	16,872	0·94	,,

Cattle.

1882	35,654	127	22,916	22	12	48	82	0·35	5%
1883	26,453	130	20,501	17	1	46	64	0·31	,,
1884	33,900	139	22,616	20	13	52	85	0·37	,,
1885	34,000	192	21,073	32	8	67	107	0.50	,,
1886	39,154	135	22,113	18	7	39	64	0·29	,,
1887	48,484	148	28,083	23	18	68	109	0·39	,,
1888	34,464	61	10,920	8	4	35	47	0·43	,,
1889	32,251	68	11,610	14	7	31	52	0·45	,,
1890	33,965	71	11,057	5	4	14	23	0·21	,,
1891	40,736	68	10,476	6	4	4	14	0·13	,,
1892	41,609	71	9,757	8	3	15	26	0·26	,,
1893	38,154	45	9,840	4	1	13	18	0·18	,,
Total	438,824	1,255	200,962	177	82	432	691	0·34	,,

thing goes wrong with the herds, they do not fail to let us know it at once by special letters.

Anyhow, thanks chiefly to new veterinary surgeons who do send reports, we see that in the twelve years, up to January 1st of this year, we have had exact returns as to 1,788,879 sheep and 200,962 cattle—about half of all those that were vaccinated.

The mortality among sheep and cattle is slightly higher after the first vaccination than after the second. This fact seems to us easy to explain. The animals reported dead include both those that died as the result of the vaccinations, and those that, being already infected at the time, died of the actual disease. But, at the time of second vaccination, the animals are already more or less protected : hence a lower mortality from the actual disease, and a lower sum total.

The whole loss of sheep is about 1 per cent. : the average for the twelve years is 0·94. So we may say that *the whole average loss of vaccinated sheep, whether from vaccination or from the disease itself, is about 1 per cent.* The loss of vaccinated cattle is still less : for the period of twelve years, it is 0·34, or about ⅓ per cent.

These results are extremely satisfactory. It is to be noted especially that the average annual death-rate from *charbon*, before vaccination—the average given in these reports—is estimated at 10 per cent. among sheep, and 5 per cent. among cattle. But even if we put it at 6 per cent. for sheep, and 3½ per cent. for cattle, and say that the worth of a sheep is 30 francs, and of an ox or a cow 150 francs—which is well below their real value—even then it is obvious that the advantage of these vaccinations to French agriculture is about five million francs in sheep and two million in cattle. And these figures are rather too low than too high.

2. Rouget.

Some years after the discovery of vaccination against *charbon*, M. Pasteur discovered the vaccines for a disease of swine known under the name of *rouget*. From 1886, these vaccines were prepared and sent out under the same conditions as the vaccines against *charbon*. The following table gives the reports that have come to us of this disease[1]:—

VACCINATION AGAINST ROUGET (FRANCE).

Years.	Total number of animals vaccinated.	Number of Reports.	Animals vaccinated according to reports received.	Mortality.			Total.	Total loss per 100.	Average loss before vaccination.
				After first vaccination.	After second vaccination.	During the rest of the year.			
1886	For these two years France and other countries are put together.	49	7,087	91	24	56	171	2·41	20%
1887		49	7,467	57	10	23	90	1·21	"
1888	15,958	31	6,968	31	25	38	94	1·35	"
1889	19,338	41	11,257	92	12	40	144	1·28	"
1890	17,658	41	14,992	118	64	72	254	1·70	"
1891	20,583	47	17,556	102	34	70	206	1·17	"
1892	37,900	38	10,128	43	19	46	108	1·07	"
Total	111,437	296	75,455	534	188	345	1,067	1·45	"

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[1] The reports for 1893 are at present too few to be utilised for this table.

The total average of losses during the past seven years is 1·45 *per cent. or about* 1½ *per cent.*

This average is appreciably higher than the average for *charbon*. But it must be noted that the mortality from *rouget* among swine, before vaccination, was much higher than that from *charbon* among sheep. It was about 20 per cent.; a certain number of reports speak of losses of 60 and even 80 per cent.: so that almost all the veterinary surgeons are loud in their praises of the new vaccination.

The rest of M. Chamberland's paper is concerned with the defects, such as they are, of the vaccinations, and the need of absolute cleanliness in the making of them: which is somewhat difficult for this vast number of vaccinations of animals all over France.

Anthrax in man is happily a rare disease, and not always fatal; still, it is common enough among those who are exposed to the infection: three deaths lately at Worcester, and the recent cases at the General Post Office. Under treatment with *sérum anti-charbonneux*, Salvatore has lately recorded fourteen successful cases (*Brit. Med. Journ.*, July 30, 1898), and another observer has recorded seven successful cases.

IV

TUBERCLE

BEFORE Laennec, tubercle had been taken for a degenerative change of the tissues, much like other forms of degeneration. It was Laennec who brought men to see that it is a disease of itself, different from anything else; and this great discovery of the specific nature of tubercle, and his invention of the stethoscope, place him almost level with Harvey. He founded the facts of tubercle, and on that foundation Villemin built. In 1865, Villemin communicated to the Académie des Sciences his discovery that tubercle is an infective disease; that he had produced it in rabbits, by inoculating them with tuberculous matter. *En voici les preuves*, he said. He appealed to these inoculations to prove his teaching :—

> *La tuberculose est une affection spécifique.*
> *Sa cause réside dans un agent inoculable.*
> *L'inoculation se fait très-bien de l'homme au lapin.*
> *La tuberculose appartient donc à la classe des maladies virulentes.*

It was no new thing to say, or to guess, that phthisis was or might be infective. So far back as 1500, Frascatorius had said that phthisis came "by the gliding of the corrupt and noisome humours of the patient into the lungs of a healthy man." Surely, if clinical experience could suffice, men would have made something out of this wisdom of Frascatorius. They made nothing of it; they waited three centuries for Villemin to inoculate the rabbits, and then the thing was done—*En voici les preuves.* Three years later, Chauveau produced the disease in animals, not by inoculation, but by the admixture of tuberculous matter with their food. Then, as the work grew, there came a short period of uncertainty: different species of animals are so widely different in their susceptibility to the disease that the results of further inoculations seemed to go against Villemin; and it was not till 1880 that Cohnheim finally established Villemin's teaching, and even went beyond it, making inoculation the very proof of tubercle:—

> "Everything is tuberculous, that can produce tuberculous disease by inoculation in animals that are susceptible to that disease: and nothing is tuberculous, that cannot do this."

And then, in 1881, came the welcome news that Koch had discovered the bacillus of tubercle: "Henceforth in our warfare we have to reckon not with a nameless something, but with a definite parasite. . . .

Before all things, we must shut off the sources of the infection."

In 1890, the first battle was fought, and was lost. The date of the announcement of *tuberculin* in the *Deutsche Medizinische Wochenschrift* is November 15, 1890. Its failure was one of the world's tragedies; but the defeat may not be final. We may live to see phthisis fought, and beaten, with its own weapons: anyhow, there are other ways of fighting it. But phthisis is only one of many tuberculous diseases. Apart from it, see how the whole study of tuberculosis, and the prevention of it, have come from the work of Villemin, Chauveau, and Koch. Out of the recent literature on this subject, take the articles in the *Practitioner*, June, 1898; the reports of the Fourth Congress on Tuberculosis (Paris, July and August, 1898); and Professor Delépine's lecture at Sudbury (Lord Vernon's farm) on Tuberculosis and the Milk Supply (*Lancet*, September 17, 1898). It is true that the diminution of tuberculosis, in this country, began before bacteriology, thanks to improved methods of drainage and sanitation:[1] but see what bacteriology has done since 1882, in every civilised country in the world.

1. It has given people a more reasonable and more hopeful idea of the whole subject:—

"From the public health point of view, the tubercle-bacillus must be looked upon as the *fons et origo mali*: and all statistics that have recently been collected go to prove that the tubercle-bacillus does its work, as a rule, in the post-natal period. Hereditary tuberculosis may be left out of account: for, although there may be a few cases of congenital tuberculosis, all statistics point to the fact that tuberculosis is a disease which is contracted after birth—a most comforting knowledge for families in which tuberculosis has been rife.[1] . . . Weakness of the tissues, which of course may be inherited, may be a predisposing cause: but without the exciting cause, the tubercle-bacillus, there can be no tuberculosis." (*Practitioner*, *loc. cit.*)

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[1] See on this point Dr. Arthur Ransome's "Researches in Tuberculosis" (Weber-Parkes Prize Essay, 1897), and Sir Hugh Beevor's recent monograph.

2. The tubercle-bacillus, found in the sputa, or in the discharges, or in a particle of tissue, is evidence that the case is tuberculous: a right diagnosis is made at an early stage of the disease.

3. Bacteriology has proved, beyond all reasonable doubt, that *tabes mesenterica*, a tuberculous disease that kills thousands of children every year in this country,[2] is due in great measure to infection from the milk of tuberculous cows.

4. It has taught people that the sputa of phthisical patients are a most common source of infection: and it has profoundly influenced the rules for the care and nursing of such cases.

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[1] In that very clever novel, "The Open Question," the husband and wife drown themselves, by mutual consent, lest their unborn child should be consumptive: thus killing three people for fear one of them should die.

[2] In 1895, the deaths from this disease in England were 7,389, of whom 3,855 were under a year old.

5. It has brought about the present rigorous control of the meat and milk trades:—

"Thirty years ago, that is about three years after Villemin, Chauveau demonstrated experimentally that tuberculosis could be induced in cattle by feeding them on tuberculous products. Nearly thirty years have been necessary, to allow public opinion to come to the conclusion that these men of science were right. In the Reports of the last two Royal Commissions on Tuberculosis we find the following statement: 'No doubt the largest part of the tuberculosis which man obtains through his food is by means of milk containing tuberculous matter.'"[1] (Professor Delépine, *loc. cit.*)

"Quite 75 per cent. of all meat seized under the Public Health Acts is condemned on account of tubercle. I have seen, and not uncommonly, animals in good condition, fat and firm, and carrying plenty of flesh, that have had to be condemned after being slaughtered. . . . In Copenhagen slaughter-houses, for 1890–93 inclusive, the percentage of tuberculous animals was 17·7 for oxen and cows, and 15·3 for swine; in Berlin slaughter-houses, 1892–93, the percentage for oxen and cows was 15·1; in Edinburgh, of 900 milch-cows slaughtered in 1890 no less than 40 per cent. were found tuberculous." (Dr. Robinson, *Quarterly Medical Journal*, July, 1897.)

"In Victoria, the number of cattle found to be affected with tubercle when slaughtered is very small compared to other countries, being only 4 per cent., as against 15 per cent. in Berlin, 17·7 per cent. in Denmark, 20 per cent. in France, 22 in Saxony, and 25 in England. This result is attributed to systematic inspection; which is to be made still more rigorous." (*Lancet*, January 28, 1899.)

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[1] For facts about tuberculous milk, see Appendix. Also Reports of the Royal Commission on Tuberculosis (1896–98); Sir Richard Thorne Thorne's Harben Lectures (1898); the Report on the Cambridge Milk Supply, by Professor Kanthack and Dr. Sladen (*Medical Press*, January 18, 1899); and the Report on the Liverpool Milk Supply, by Professor Woodhead and Dr. Cartwright Wood (*Lancet*, February 11, 1899). For facts about tuberculous meat, see *Lancet*, February 28, 1899.

6. Tuberculin (Koch's fluid) is now in general use for the detection of tuberculosis in cattle, to "shut off the sources of the infection." A full account of this method, in different countries, was given by Professor Bang, of Copenhagen, at the Fourth Congress on Tuberculosis, Paris, 1898:—

"In cattle, an injection of 1 to 2 cubic centimetres, according to the strength of the preparation, into the neck, is followed in 8–12 hours by a rise in temperature of 2, 3, or 4 degrees, if the animal is tuberculous; if it be healthy, there is no rise in temperature, or only an insignificant one. That the test is of great value, the following details and experiments of recognised authorities will prove.

"Professor McFadyean, in the Report of the Royal Commission on Tuberculosis, says: 'I have no hesitation in saying that, taking full account of its imperfection, tuberculin is the most valuable means of diagnosis in tuberculosis that we possess.'[1]

"A. Eber, of the Veterinary College at Dresden, experimented on 174 beasts, and found that 136, or 78·2 per cent., gave a typical reaction with tuberculin; 6, or 3·4 per cent., gave a doubtful reaction, a rise of 1 or 1½ degrees; while 32, or 18·4 per cent., did not react. Of the 136 beasts which gave a typical reaction, 22 were slaughtered, and, in all these, tuberculous lesions were found; of the 6 doubtful cases, 3 were slaughtered, and, in 2, tuberculous lesions were found; while of the 32 which did not react, 3 were slaughtered, and were found to be free from tuberculosis."

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[1] "I have most implicit faith in tuberculin as a test for tuberculosis, when it is used on animals standing in their own premises and undisturbed. It is not reliable when used on animals in a market or slaughter-house. A considerable number of errors at first were found when I examined animals in slaughter-houses after they had been conveyed there by rail, &c. Since that, using it on animals in their own premises, I have found that it is practically infallible. I have notes of one particular case, where 25 animals in one dairy were tested, and afterwards all were killed. There was only one animal which did not react, and it was the only animal not found to be tuberculous when killed." (Professor McFadyean.)

"Professor Bang, of Copenhagen, injected 80 tuberculous animals with tuberculin: of these, 73 gave a typical reaction, 2 gave a doubtful reaction, and 5 did not react. In the 2 which gave a doubtful reaction, the tuberculous lesions were very slight; in the 5 which did not react, the signs of the tubercle were slight, and not of recent date."[1] (*Hewlett*, 1895.)

Thus from the facts of bacteriology have come the present methods for the prevention of phthisis and other forms of tuberculous infection, the rules for the nursing of phthisical patients, and some part of the treatment of tuberculosis, especially in those cases that are not medical but surgical. The "old tuberculin" of 1890, that failed to cure patients who were already infected, succeeds in preventing the infection of healthy infants.

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[1] The latest figures to hand refer to the testing of 270 cows on some farms in Lancashire. Of these cows, 180 reacted to the tuberculin test, 85 did not react, and 5 were doubtful. Tuberculous disease was actually found in 175 out of the 180 = 97·2 per cent. (See *Lancet*, August 5, 1899.) It will be remembered that Her Majesty the Queen, last winter, sanctioned the destruction of 36 out of 40 of the dairy cows at the Windsor Farm, because they had reacted to this test. "A new dairy herd is being obtained for the Queen's Home Farm, all the animals for it being tested, and admitted to the herd only when they do not react. (*British Medical Journal*, April 22, 1899.)

V

DIPHTHERIA

THE bacillus of diphtheria, the Klebs-Loeffler bacillus, was first described by Klebs in 1875; and was first obtained in pure culture by Loeffler in 1884. Its isolation was a matter of great difficulty, and the work of many years, because of its association in the mouth with other species of bacteria.[1] The use of the antitoxin is not yet seven years old: it was

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[1] The following list of organisms found in 353 cases of diphtheria is a good instance of the practical difficulties of the work:—

"In 216, the diphtheria-bacillus was found alone. In the remaining 137, it was associated with the following organisms:—

Streptococci	6
Staphylococci	55
Bacilli	19
Torulæ	9
Sarcinæ	6
Streptococci and micrococci	2
Micrococci and bacilli	9
Streptococci and bacilli	1
Torulæ and bacilli	1
Micrococci and sarcinæ	6
Micrococci and torulæ	4
Many forms present together	19
	137

(Hewlett, *Manual of Bacteriology.*)

December, 1890, when the news came that Behring and Kitasato had at last cleared the way :—

> "Our researches on diphtheria and on tetanus have led us to the question of immunity and cure of these two diseases ; and we have succeeded in curing infected animals, and in immunising healthy animals, so that they have become incapable of contracting diphtheria or tetanus."

Aronsen, Sidney Martin, Escherich, Klemensiewicz, and other men, were working on the same lines ; and in 1893 Behring and Kossel, and Heubner, published the first cases treated with antitoxin. Then, in 1894, came the Congress of Hygiene and Demography at Budapest, and Roux's triumphant account of the good results already obtained.

There is no room here for statistics from all parts of the world, and no need to praise diphtheria-antitoxin. At first, it was hard to believe the full wonder of the discovery : the medical journals of 1895 and 1896 contain the fossils of criticism—general impressions, apprehensions, first opinions, all the *may be* and *must be* of the earlier debates on the new treatment.[1] To get at the truth we must reckon in thousands : take, out of a whole mass of evidence, all just alike, the reports from Berlin, Munich, Vienna, Strasbourg,

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[1] The finest of all the fossils is from the *Saturday Review*, February 2, 1895: "*It is a pity that the English press should continue to be made the catspaw of a gang of foreign medical adventurers.*" This and other good specimens will be found embedded in *Antivivisection Evidences*.

Cairo, Boston, and New York: these to begin with. Or the following facts, cut almost at random out of the medical journals:—

"The medical report of the French army states that since the introduction of the serum-treatment of diphtheria, the mortality among cases of that disease had fallen from 11 per cent. to 6 per cent." (*Brit. Med. Journ.*, September 3, 1898.)

"Professor Krönlein (Zürich) exhibited statistical tables, showing that the prevalence of diphtheria in the canton of Zürich had been nearly uniform during the past fifteen years; and that the mortality rapidly decreased as soon as antitoxic serum was used on a somewhat large scale. In his clinic, all the patients were examined bacteriologically, and serum was administered in every case of diphtheria without exception. Of 1,336 cases treated before the serum-period, 554=39·4 per cent. died; whilst during the serum-period there were 55 deaths among 437 cases =12 per cent. In cases of tracheotomy, the death-rates before and during the serum-period were 66 and 38·8 per cent. respectively." (*Lancet*, May 7, 1898, report of German Surgical Congress at Berlin.)

"Dr. Kármán was entrusted by the Hungarian Government with the task of instituting measures for preventing the spread of diphtheria in a village and its neighbourhood. As general hygienic regulations accomplished nothing, he tried preventive inoculation. . . . Among 114 children thus treated, there was during the next two months no case of diphtheria, although the disease was prevalent in the village up to the date at which inoculation commenced, and continued to rage in the surrounding villages afterwards. During those two months, only one case of diphtheria appeared in the village, and that was in an uninoculated child; while, in the previous five months, 18·3 per cent. of the village children had been attacked, of whom eight died, six not having been treated with serum. Considering the wretched hygienic condition of the village, the harmlessness of preventive inoculations, and the continuance of the disease in the neighbouring villages, where diphtheria-vaccination was not carried out, the extraordinary value of the inoculations, in the prophylaxis of diphtheria, can hardly be denied."[1] (*Brit. Med. Journ.*, January 16, 1897.)

"The most striking confirmation of the value of antitoxin has been afforded where the supply ran short during an epidemic. In Baginsky's clinic, the interruption of the serum-treatment promptly raised the mortality from 15·6 to 48·4 per cent." (*Brit. Med. Journ.*, October 20, 1895.)

"In an analysis of the ratio of mortality in 266 German cities of about 15,000 inhabitants, it was found that the ratio of mortality per 100,000 of the living, before antitoxin was used, varied from 130 to 84 from 1886 to 1893, while the ratio from 1894 to 1897 varied from 101 to 35. It is a significant fact that during 1894, when although antitoxin was used to a certain extent it was not in general use, the ratio was 101; that when antitoxin was used more extensively, in 1895, the ratio was 53; that in 1896 it was 43; that in 1897, when antitoxin was very generally used, the rate fell to 35." (*Trans. Massachusetts Med. Soc.*, 1898.)

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[1] For this use of the antitoxin, to stop an outbreak of diphtheria in a village or a school or a family, see among other reports those of Dr. Twombly and Dr. Morrill, in the *Boston Medical and Surgical Journal*, December, 1897, and March, 1898. Also the report from the Charité Hospital in Berlin, quoted in the *Lancet*, April 2, 1898; and an account of an outbreak among 60 children in an Institute. (*Lancet*, January 28, 1899.)

And, of course, there is a multitude of reports from private practice, giving the lowest death-rate of all, because the children are in favourable circumstances. But the final evidence is in the larger statistics; and, of all the vast literature on the diphtheria-antitoxin, the place of honour in this country should be given to Dr. Cobbett's memoir on the Reports of the Metropolitan Asylums Board, in the *Lancet*, December 3, 1898, and to Dr. Goodall's final statement of these Reports in the *Brit. Med. Journ.*, February 4, 1899. Beside these, there are three reports of especial interest—from the American Pædiatric Society, the Paris Hospital for Sick Children, and the Clinical Society of London.[1]

I

Report of the American Pædiatric Society's Collective Investigation into the use of Antitoxin in the treatment of diphtheria in private practice. (Eighth Annual Meeting, Montreal, May, 1896.) From the *New York Medical Record*, July 4, 1896.

This vast collection of cases is of special interest, because they occurred in private practice. In most of them the nature of the disease was proved by bacteriological examination; in the rest, the clinical evidence was decisive: "It is possible that among the latter we have admitted some streptococcus cases, but the number of such is certainly very small." All other doubtful cases, 244 in number, were excluded.

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[1] One of the latest reports, and one of the best, is Dr. Herman Biggs' paper at the New York Academy of Medicine, giving the results in New York, since 1895. See the *New York Medical Record*, March 4, 1899.

Three thousand three hundred and eighty-four cases were reported by 613 physicians from 114 cities and towns, in fifteen different States, the District of Columbia, and the Dominion of Canada. To these 3,384 cases were added 942 cases from tenement-houses in New York, and 1,468 cases from tenement-houses in Chicago. The New York and Chicago cases were, most of them, treated by a corps of inspectors of the Health Board of the city ; and the municipal surveillance was very strict at Chicago :—

> "There are very few hospitals in America that receive diphtheria patients. . . . It was the custom in Chicago to send an inspector to every tenement-house case reported, and to administer the serum unless it was refused by the parents. These cases were therefore treated much earlier, and the results were correspondingly better than were obtained in New York, although the serum used was the same in both cities, viz., that of the New York Health Board."

The sum total of results was 5,794 cases with 713 deaths = 12·3 per cent., including every case returned ; but 218 were moribund at the time of injection or died within twenty-four hours of the first injection. "Should these be excluded, there would remain 5,576 cases, in which the serum may be said to have had a chance, with a mortality of 8·8 per cent."

Of	996	cases injected	on the first	day of the disease,	49	died =	4·9	p.c.
,,	1,616	,, ,,	,, second	,, ,,	120	,, =	7·4	,,
,,	1,508	,, ,,	,, third	,, ,,	134	,, =	8·8	,,
,,	758	,, ,,	,, fourth	,, ,,	147	,, =	20·7	,,
,,	690	,, ,,	on or after the fifth	,,	244	,, =	35·3	,,

And in 232 cases, where the day of injection was unknown, there were 19 deaths = 8·2 per cent.

"No one feature of the cases of diphtheria treated by antitoxin has excited more surprise among the physicians who have reported them than the prompt arrest, by the timely administration of the serum, of membrane which was rapidly spreading downward below the larynx. Such expressions abound in the reports as 'wonderful,' 'marvellous,' 'in all my experience with diphtheria have never seen anything like it before,' &c.

"Turning now to the operative cases, we find the same remarkable effects of the antitoxin noticeable. Operations were done in 565 cases, or in 16·7 per cent. of the entire number reported. Intubation was performed 533 times, with 138 deaths, or a mortality of 25·9 per cent. In the above are included nine cases in which a secondary tracheotomy was done, with seven deaths. In 32, tracheotomy only was done, with 12 deaths, a mortality of 37·4 per cent. Of the 565 operative cases, 66 were either moribund at the time of operation or died within twenty-four hours after injection. Should these be deducted, there remain 499 cases operated upon, by intubation or tracheotomy, with 84 deaths, a mortality of 16·9 per cent.

"Let us compare the results of intubation, in cases in which the serum was used, with those obtained with this operation before the serum was introduced. Of 5,546 intubation cases in the practice of 242 physicians, collected by McNaughton and Maddren (1892), the mortality was 69·5 per cent. Since that time, statistics have improved materially by the general use (in and about New York, at least) of calomel fumigations. With this addition, the best results published (those of Brown) showed in 279 cases a mortality of 51·6 per cent.

"But even these figures do not adequately express the benefit of antitoxin in laryngeal cases. Witness the fact that over one-half the laryngeal cases did not require operation at all. Formerly, ten per cent. of recoveries was the record for laryngeal cases not operated upon. Surely, if it does nothing else, the serum saves at least double the number of cases of laryngeal diphtheria that has been saved by any other method of treatment."

II

The report from the Hospital for Sick Children, Paris, is contained in a memoir, *Sérum-Thérapie de la Diphtérie*, the joint work of MM. Roux, Martin, and Chaillon (*Annales de l'Institut Pasteur*, September, 1894). It gives the results of the serum-treatment during February–July, 1894. The cases were not selected: the antitoxin was given in every case that was proved, by bacteriological examination, to be diphtheria—with the exception of 20 cases where the children were just dying when they were brought to the hospital. No change was made either in the general treatment or in the local applications to the throat; these were the same that had been used in former years: *le sérum est le seul élément nouveau introduit.*

In 1890–1893, before the serum-treatment, 3,971 children were admitted to the diphtheria wards; and 2,029 of them died. The percentage of these deaths was—

In 1890	55·88	Average = 51·71.
,, 1891	52·45	
,, 1892	47·64	
,, 1893	48·47	

The serum was used from February 1 to July 24, 1894. During this period 448 children were admitted, of whom 109 died = 24·5.

During the same period (February-June) the Trousseau Hospital, where the serum was not used, had 520 cases, with 316 deaths = 60·0.

The cases at the Hospital for Sick Children must be divided into those that required tracheotomy and those that did not require it:—

MORTALITY AMONG CASES NOT REQUIRING TRACHEOTOMY.

In 1890	47·30	Average = 33·94.
„ 1891	46·64	
„ 1892	38·8	
„ 1893	32·02	

During the serum-period, the mortality of these cases was 12·0. At the Trousseau Hospital, without the serum, the mortality of these cases, during the same period, was 32·0.

MORTALITY AMONG CASES REQUIRING TRACHEOTOMY.

In 1890	76·35	Average = 73·49.
„ 1891	68·36	
„ 1892	74·6	
„ 1893	73·45	

During the serum-period, the mortality of these cases was 49·0. At the Trousseau Hospital, without the serum, the mortality of these cases, during the same period, was 86·0.

Setting aside, out of the 448 children, those cases of "membranous sore throat" or "pseudo-diphtheria," in which the Klebs-Loeffler bacillus was not found, there remain 320 cases where it was found. Of these 320 children, 20 were just dying on admission, and did not receive the serum. Of the 300 who received it, 78 died = 26·0. Before the serum-period, the mortality of these cases at the same hospital was about 50·0. The complications of diphtheria, such as paralysis, were much less frequent during the serum-period than they had been before it.

III

In 1898, the Clinical Society published the Report of their Special Committee, based on 663 cases (*Trans. Clin. Soc.*, xxxi., 1898, pp. 1–50). The whole report should be read carefully: but there is room here for nothing more than the latter part of it. This is given at length.

A

TABLE SHOWING THE GENERAL MORTALITY OF CASES TREATED, *ON THE SAME DAY OF THE DISEASE*, WITH AND WITHOUT ANTITOXIN.

ANTITOXIN COMMITTEE: 633 cases treated with Antitoxin.				METROPOLITAN ASYLUMS BOARD, 1894: 3,042 cases treated without Antitoxin.				Difference of percentage.
Day of the disease on which treatment was begun.	Cases.	Deaths.	Mortality per cent.	Day of admission to hospital.	Cases.	Deaths.	Mortality per cent.	
1st	20	2	10·0	1st	133	30	22·5	12·5
2nd	92	10	10·8	2nd	539	146	27·0	16·2
3rd	133	20	15·0	3rd	652	192	29·4	14·4
4th	130	26	20·0	4th	566	179	31·6	11·6
5th and after.	258	66	25·5	5th	1,152	355	30·8	5.3
Totals	633	124	19.5	Totals	3,042	902	29·6	10·1

DIPHTHERIA

B

Summary and Conclusions of the Committee's Report.

"The material for the investigation of the clinical value of the antitoxin serum in the treatment of diphtheria was not obtained from selected, but from consecutive, cases, reported from the general hospitals and the fever hospitals of the Metropolitan Asylums Board; all were made use of which fulfilled the requirements of the Committee.

"The Committee rejected all cases in which satisfactory proof of the existence of true diphtheria was not shown, either by the presence of the *Bacillus diphtheriæ* upon bacteriological examination, or by the occurrence of paralysis in the course of the illness. All were also rejected in which the amount of antitoxin administered was stated in cubic centimetres and not in normal units, the Committee having no means by which the strength of the antitoxin could in these cases be determined.

"Six hundred and thirty-three cases form the basis on which the report is drawn up; 549 were treated with antitoxin obtained from the laboratory of the Royal Colleges of Physicians and Surgeons; the remainder, 84 in number, were injected with antitoxin obtained from other sources. In 9 instances, antitoxin from two different sources was injected into the same patient.

"Statistics of the disease before the use of antitoxin are introduced as control series; these were obtained from the fever hospitals of the Metropolitan Asylums Board, and from the general hospitals; and, like the antitoxin series, are compiled from consecutive and not from selected cases.

"The general mortality, under the antitoxin treatment, was 19·5 per cent.; a reduction of 10 on the percentage mortality of the cases treated in the hospitals of the Metropolitan Asylums Board in 1894. If 15 fatal cases, in which death took place within twenty-four hours of the first injection, be deducted, the mortality falls to 15·6 per cent.; which is very little more than half the mortality during 1894 under other forms of treatment.

"The lessened mortality is especially noticeable in the earlier years of life, the percentage mortality of children under five being 26·3, as opposed to 47·4. In the next period of five years, the percentage of mortality is 16·0, as opposed to 26·0; whilst after ten years of age the difference in the mortality is slight.[1]

"Laryngeal diphtheria is admittedly the most dangerous form. The laryngeal cases have a percentage mortality of 23·6 in the antitoxin, as compared with 66·0 in the non-antitoxin series. In the cases in which laryngeal symptoms are so severe as to necessitate tracheotomy, the saving of life by the use of antitoxin is very marked, the mortality being

[1] After this period, the disease is much less fatal.

reduced one-half, to 36·0 as opposed to 71·6 per cent.

"The strongest evidence of the value of the antitoxin treatment is that in addition to reducing the general mortality by one-third, the duration of life in the fatal cases is decidedly prolonged. These two facts taken together conclusively prove the beneficial effects of the antitoxin treatment.

"The incidence of paralysis[1] is greater in the antitoxin than in the control series. This increased number is partly explained by the lessened mortality, and partly by the longer duration of life in the fatal cases affording time for the development of paralytic symptoms. The percentage mortality of those who had some form or other of paralysis is lower in the antitoxin than in the control series; so that notwithstanding the apparent greater risk of paralysis supervening, the probability of final recovery is greater.

"No definite conclusion can be drawn, for the reasons stated in the body of the report, as to the advantage of administering the whole of the antitoxin within forty-eight hours of the first injection, or continuing it for a longer period; but evidence is afforded of the importance of its administration as early as possible in the course of the disease: the percentage mortality in cases injected on the first and second days of the disease being 10·7, as compared with 25·5 for those first receiving the injection on the fifth or some subsequent day.

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[1] Post-diphtheritic paralysis, in the great majority of cases, is limited to a very narrow area, *e.g.*, the soft palate, or the small muscles of the eye; and usually disappears after convalescence.

"No conclusion can be drawn, from the cases reported on, as to the amount of antitoxin which should be used to produce the best effects; but they show that the administration of very large doses is followed by no pronounced ill effects.

"The injection of antitoxin is responsible for the production of rashes, joint-pains, and possibly for the occurrence of late pyrexia.[1] In 34·7 per cent. the injections were followed by rashes. Some amount of fever accompanied the rash in 60 per cent. In only 9·4 per cent. of those in whom rashes were observed did death ensue.

"Joint-pains were observed in 40, or 6·3 per cent. of the whole number, and all but five of them had a rash as well.

"In 26, or 65 per cent. of the joint-pains, some rise of temperature accompanied the pain. A rise of temperature during convalescence, accompanied by either rash or joint-pain, occurred in 27, or 4·2 per cent. of the whole number.

"No connection could be traced between the amount of antitoxin administered and the occurrence of rashes or late pyrexia, but the pain in and about the joints appears to have a relationship to the amount of antitoxin used.

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[1] Since the date of this Report, much has been done to obviate these faults of the serum-treatment. Take, for instance, M. Spronck's paper in the *Annales de l'Institut Pasteur*, October, 1898: "Influence favorable du chauffage du sérum antidiphtérique sur les accidents post-thérapiques;" or the earlier paper, on the same subject, by MM. Béclère, Chambon, and Ménard.

"The results of the Committee's investigation tend to show that by the use of antitoxin—

1. The general mortality is reduced by one-third.
2. The mortality in tracheotomy falls by one-half.
3. Extension of membrane to the larynx very rarely occurs after the administration of antitoxin.
4. The duration of life in the fatal cases is decidedly prolonged.
5. The number of fatal cases is less when antitoxin is used early in the illness than in those which do not receive it until a later period.
6. The frequency of the occurrence of paralysis is not diminished, but the percentage of recoveries in cases with paralysis is slightly increased.[1]
7. Rashes are produced in about one-third of the cases, and are attributable to the antitoxin.

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[1] For an exhaustive and final study of the diphtheritic paralyses, see Dr. Woollacott's recent essay in the *Lancet*, August 26, 1899: "The use of antitoxic serum in the treatment of diphtheria has, up to the present time, in the London fever hospitals, had two main results—the death-rate has fallen, while the paralysis-rate has risen. In the hospitals of the Metropolitan Asylums Board, the former has been reduced from 29 per cent. to 15·3 per cent., while the latter has risen from 13 per cent. to as high as 21 per cent. in 1896. This increase of paralysis is chiefly due to the fact that many more patients now recover from the primary disease, and live long enough for paralysis to show itself. *During the last two years, however, the occurrence of paralysis has begun to diminish in frequency. . . . The earlier antitoxin is given in diphtheria, the less likely is paralysis to follow.*" It is to be borne in mind that post-diphtheritic paralysis, in the great majority of cases, affects only a very small group of muscles; ,of Dr. Woollacott's tabulated cases, 377 were of this kind, and 97 were severe. And "the type of paralysis has, on the whole, become less severe, or at all events less dangerous to life,"

8. Pain and occasionally swelling about the joints are produced in a number of cases.

9. Even when used in large doses, no serious ill effects have followed the injection of antitoxin."

Note.

The *Lancet*, August 5th, contains an abstract of Dr. Gabritchefski's recent account of the antitoxin treatment in Russia. "He points out that in recent years the number of persons attacked by the disease has increased, the figures for the whole of Russia rising from about 100,000, or 120,000, ten years ago, to considerably over 200,000 in 1897. *The introduction of the serum treatment has however had a marked effect on the mortality of the disease; and the actual number of deaths from diphtheria has either not increased at all or has slightly diminished.*"

For further reference to the *prophylactic* value of the antitoxin see *Lancet*, February 10, 1899.

A book by Dr. Sims Woodhead, Professor of Pathology at Cambridge, is announced for publication, giving a complete account of the results obtained in the hospitals of the Metropolitan Asylums Board.

VI

TETANUS

TWENTY years ago, the cause of tetanus (lockjaw) was unknown, and men were free to believe that it was due to inflammation travelling up an injured nerve to the central nervous system. This false and mischievous theory was abolished by the experimental work of Sternberg (1880), Carle and Rattone (1884), and Nicolaier (1884); who proved, once and for all, that the disease is an infection by a specific flagellate organism. These men fought their way through a whole forest of difficulties:—

1. In some parts of the world, tetanus is so common, with or without evidence of any wound, that it may be called endemic; and this form of the disease was taken as evidence that tetanus could occur "of itself," without external infection:—

> "Tetanus is an exceedingly common disease in some tropical countries. In Western Africa, for example, a large proportion of wounds, no matter how trifling as

wounds they may be, if they are fouled by earth or dirt, result in tetanus. The French in Senegambia have found this to their cost. A gentleman who had travelled much in Congoland told me that certain tribes poison their arrows by simply dipping the tips in a particular kind of mud. A wound from these arrows is nearly sure to cause tetanus. In many countries, so general and so extensive is the distribution of the tetanus bacillus that trismus neonatorum (tetanus of newly-born infants) is a principal cause of the excessive infant mortality." (Manson, *Tropical Diseases*, 1898.)

2. The bacillus has its natural abode in the superficial layers of the soil, where it is associated with a vast number of other organisms; wherever it is found, and it is found everywhere, it is mixed with all other microbes:—

"Houston gives the estimated number of microbes per gramme found in 21 samples of soil. These vary from 8,326 in virgin sand, and 475,282 in a virgin peat, to 115,014,492 in the soil from the trench of a sewage farm. . . . Among the ubiquitous organisms which are habitually found in earth is the bacillus of tetanus. It is said to be present in almost all rich garden-soils, and that the presence of horse-dung favours its occurrence. There seems to be no doubt as to the ubiquity of the tetanus germ." (Poore, *Milroy Lectures*, 1899.)

3. The bacillus of tetanus, since it thus flourishes below the earth, away from the air, cannot be got to grow in cultures exposed to the air: it is "strictly anaërobic," and must be cultivated below the surface

of certain nutrient media, or in an atmosphere of nitrogen or hydrogen.

With these and other difficulties in the way, no wonder that it took some years to prove the true pathology of tetanus. The final success of the work was mainly due to Nicolaier. He started from the well-known fact that tetanus most often comes of wounds or scratches contaminated with particles of earth—such mischances as the grinding of dirt or gravel into the skin, or the tearing of it by a splinter of wood or a rusty nail :—

> "Every child who falls on the ground and gets an abrasion of the skin, all tillers of the soil who get accidental wounds in the course of duty, and every horse which 'breaks its knees' by falling in the London streets, runs potentially a risk of inoculation with tetanus. . . . A review of the main facts connected with tetanus cannot but rouse in us some surprise that, in face of the ubiquity of the cause, the disease in man should be so rare. This is probably in part due to the fact that we wear boots." (Poore, *loc. cit.*)

Nicolaier therefore studied the various microbes of the soil, and made inoculations of garden-mould under the skin of rabbits. He was able, by these inoculations, to produce tetanus in them ; and the discharge from the points of inoculation, put under the skin of other rabbits, produced the disease again. He also identified the bacillus, and cultivated it ; but in these cultures it was mixed with other organisms, and he failed to isolate it from them. Carle and Rattone, and Rosenbach, were able to produce tetanus in animals by inoculating them with discharge from the wounds of tetanic patients. Finally, Kitasato, in 1889, obtained pure cultures of the bacillus. Beginning with impure cultures such as Nicolaier had made, he kept these at a temperature of 36° C. till the bacillus had spored; then, by repeated exposures of the cultures to a temperature of 80° C. for three-quarters of an hour at a time, he killed off all organisms except the spores of the tetanus-bacillus; then he kept these in an atmosphere of hydrogen, at a temperature of 20° C., and thus got pure cultures.

Brieger, Fränkel, Cohn, Sidney Martin, and others, have studied the chemical products of the disease, have obtained them from cultures and from infected tissues, and have been able, with these toxins, to produce tetanus. Further, it has been proved that the bacillus does not tend to invade the blood, or to pass beyond the lymphatic glands in the immediate neighbourhood of the wound; it stays in and about the wound, grows there, and pours thence into the blood the chemical products of its growth, which have a selective action, like a dose of strychnine, on the cells of the central nervous system.

It is evident that the truth about tetanus was found, proved, and interpreted by experiments on animals. The old fancies that the disease was an acute inflammation running up a nerve are gone for ever:

men know, at last, what tetanus is. For the practical use of this knowledge, consider this great difficulty, that the disease is latent and unrecognised till it is fulminant: the first sign of it is the last stage of it; there may be no warning, nothing but a trivial wound, till the central nervous system is affected. Besides, the work is all new, still in the making; it is too soon to ask for final results in practice, when science has hardly done speaking. Yet the results are there already, and more to come: *nos méthodes se perfectionnent de jour en jour*:—

1. It has become common knowledge that lockjaw is the result of inoculation of the skin with earth or dirt containing a specific organism; the old notions that a clean cut between the thumb and the forefinger was especially dangerous, that a poultice made a dirty cut clean, and the like, are giving way to a thorough cleansing and antiseptic dressing of all such wounds. Certainly, with tetanus, prevention is better than cure; and the risk of an earth-fouled wound is most surely obviated by very careful cleansing, disinfection, and dressing. At the time of the Chicago Exhibition, the Medical Bureau of the Exhibition had to treat 202 cases of lacerated wounds of the hand among the workmen who unpacked the nailed-up crates. All these wounds were dressed at once by the antiseptic method, and no case of tetanus occurred. But this year (1899) the Fourth of July festivities in the United States were the cause of many cases: no less than 83 deaths from tetanus were reported, 26 of them in

and around New York. Almost all of them were due to gunshot wounds of the hand with toy-pistols: the unclean wad of the cartridge penetrated deep into the tissues of the unclean hand, taking the germs of tetanus with it, out of the reach of surgical disinfection.

But now, in the routine of hospital work, tetanus has become so rare, thanks to the antiseptic method, that a student may complete his course, and not see a case of it. Fifty years ago, among the wounded in war, it was terribly common.

2. Various preparations of curative serum have been made from immunised animals, and have given very hopeful results. The ordinary mortality of traumatic tetanus has been estimated at "nearly 90 per cent."; but this estimate is probably excessive: moreover, the disease is very variable in its intensity. The use of anti-tetanus serum does not exclude other methods of treatment. But the whole thing is too recent, and the figures too small, for final or exact estimate.[1]

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[1] In 1895, 42 cases of the antitoxin treatment were collected, with 27 recoveries. The *Journal of the American Medical Association*, November 13, 1897, gives 26 cases, with 12 recoveries. In the *Münchener Medicinische Wochenschrift* of the same week (November 16th) Weischer gives 98, with 57 recoveries. The *British Medical Journal* (July 23, 1898) 36, with 25 recoveries. Erdheim (September, 1898) 22, with 11 recoveries. Engelmann (1898) 51, with 36 recoveries. Tavel, of Berne, has lately published 10 cases, with 7 recoveries, as against 13 cases, not treated with antitoxin, of whom 11 died (*Lancet*, April 29, 1899). On the other hand, Baccelli reports even better results from another method of treatment, without antitoxin (*British Medical Journal*, 1899); but here again the figures are too small for exact judgment, nor did his method give such good results in India as in Italy (see Lieut.-Col. Henderson's paper, before the Bombay Medical Society, *Lancet*, June 3, 1899).

It is too soon (September, 1899) to know more than that the treatment is justified by results, and can be given in combination with other remedies.

3. Horses are apt to be infected by tetanus, and the antitoxin has been used in veterinary practice both for prevention and for cure. The curative results are not, at present, very striking. But as regards protection against the disease, there is evidence that horses can be immunised against tetanus, by the antitoxin, with almost mechanical accuracy. In some parts of the world the loss of horses by tetanus is a very serious matter: for instance, in St. Domingo.

(i.) *Curative.*—"Dr. Arndt, Government Veterinary Surgeon in Oppeln, has collected the cases of tetanus in horses which have up to the present been treated by Behring's antitoxin, and has published the results in the *Deutsche Med. Wochenschrift.* The first series includes 28 cases in private practice. The second series contains 28 cases treated in the Royal Veterinary Hospital in Berlin, 15 of which recovered, and 13 died; of the latter, 5 were in a hopeless state when brought to the hospital. The results of the injections are much better than those without treatment, the ordinary death-rate being about 85 per cent. In a third series of 19 horses, treated by an antitoxin of less strength, there were 16 deaths. Dr. Arndt's statistics show that of 75 horses treated, 33 recovered and 42 died. In complicated cases the remedy proved useless." (*Lancet*, March 12, 1898.)

(ii.) *Preventive.*—"The use of antitetanus serum as a preventive has been in force for some years in veterinary practice in cases of wounds or surgical procedures. To this end the Pasteur Institute has supplied 7,000 doses of antitetanus serum, a dose being 10 cubic centimetres; a quantity which has sufficed to treat preventively 3,100 animals in those parts of the country where tetanus is endemic. Among these, there has been no death from tetanus. In the case of one horse, injected five days after receiving a wound, tetanus developed, but the attack was slight. During the same time that these animals were injected, the same veterinary surgeon observed, among animals not treated by injection, 259 cases of tetanus. There would therefore seem to be no doubt of the utility of preventive injections of serum in veterinary practice." (Nocard, *Lancet*, August 7, 1897.)

4. Tetanus in man, except in some tropical countries, is a rare disease: yet a man might receive a lacerated wound under conditions especially favourable to infection; and in that case he might be able to ensure himself with a protective dose of the antitoxin. The *Lancet* of January 28th of this present year reports an outbreak of tetanus among certain obstetrical cases at Prague. It is said that the most stringent hygienic measures, including the use of antitoxin, have failed to stop this extraordinary disaster. But no details are given how the outbreak arose; and certainly, if a man were to tear his hand with any object that was especially likely to be infected with tetanus, he might do well to have recourse at once to the antitoxin to protect him.

5. The old rule, that the wounded tissues in a case of tetanus should be at once excised, has been brought into more general use. Before Nicolaier's work,

while the theory still survived that tetanus was a disease of the nerves, this rule was neither enforced nor explained.

It is only ten years since Kitasato first obtained pure cultures of Nicolaier's bacillus: yet here is a good record already of lives saved or protected. This record will be still better, in the next few years; for the want of more success is not due to any fault in the work.

It is impossible to write of tetanus without recalling Professor Kanthack's name: and his monograph on the disease remains as a landmark in pathology. An excellent account of the antitoxin treatment was given last year by Dr. Lund, of Boston, in the *Transactions of the Massachusetts Medical Society*, vol. xvii. For the intra-dural use of the antitoxin (Roux and Borrel), see Surgeon-Major Semple's paper, *Brit. Med. Journ.*, January 7, 1899.

VII

RABIES

PASTEUR'S study of rabies began in 1880; and the date of the first case treated—Joseph Meister, a shepherd-boy of Alsace—is July, 1885. The first part of the work was spent in a prolonged search for the specific microbe of rabies. It was not found: its existence was a matter of inference, but not of observation. In his earlier inoculations, he made use of the saliva of rabid animals; and M. Vallery-Radot tells the story, how Pasteur took him on one of his expeditions:—

> "The rabid beast was in this case a huge bull-dog, foaming at the mouth and howling in his cage. All attempts to induce the animal to bite, and so infect one of the rabbits, failed. 'But we *must*,' said Pasteur, 'inoculate the rabbits with this saliva.' Accordingly a noose was made and thrown, the dog secured and dragged to the edge of the cage, and his jaws tied together. Choking with rage, the eyes bloodshot, and the body convulsed by a violent spasm, the animal was stretched on a table, and

kept motionless, while Pasteur, leaning over this foaming head, sucked up into a narrow glass tube some drops of the saliva."[1]

But these inoculations of saliva sometimes failed to produce the disease; and, when they succeeded, the incubation-period was wholly uncertain: it might be some months before the disease appeared. Thus Pasteur was led to use, instead of the saliva, an emulsion of the brain or spinal cord; because, as Dr. Duboué had suggested, the central nervous system is the chief seat, the *locus electionis*, of the virus of rabies. But these inoculations also were not always successful, nor did they give a definite incubation-period.

Therefore he followed with rabies the method that he had followed with anthrax. As he had cultivated the virus of anthrax, by putting it where its development could be watched and controlled, so he must put the virus of rabies in the place of its choice. It has a selective action on the cells of the central nervous system, a sort of affinity with them; they are, as it were, the natural home of rabies, the proper nutrient medium for the virus: therefore the virus must be inoculated not under the skin, but under the skull.

These sub-dural inoculations were the turning-point of Pasteur's discovery. The first inoculation was made by M. Roux:—

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[1] But it is said, in *Antivivisection Evidences* (1895), that "Mad dogs are already so ill that they are in general very gentle"!

"Next day, when I informed Pasteur that the intracranial inoculation offered no difficulty, he was moved with pity for the dog. 'Poor beast, his brain is doubtless injured: he must be paralysed.' Without reply I went down to the basement to fetch it, and let it come into the laboratory. Pasteur did not like dogs, but when he saw this one, full of life, inquisitively rummaging about in all directions, he exhibited the greatest delight, and lavished most charming words upon it."

Henceforth all uncertainty was at an end, and the way was clear ahead: Pasteur had now to deal with a virus that had a definite period of incubation, and a suitable medium for development. The central nervous system was to the virus of rabies what the test-tube was to the virus of fowl-cholera or anthrax. As he had controlled these diseases, had turned them this way and that, attenuated and intensified them, so he could control rabies. By transmitting it through a series of rabbits, by sub-dural inoculation of each rabbit with a minute quantity of nerve-tissue from the rabbit that had died before it, he was able to intensify the virus, to shorten its period of incubation, to fix it at six days. Thus he obtained a virus of exact strength, a definite standard of virulence, *virus fixe*: the next rabbit inoculated would have the disease in six days, neither more nor less.

As he was able to intensify the virus by transmission, so he was able to attenuate it by gradual drying of the tissues that contained it. The spinal cord, taken from a rabbit that has died of rabies, slowly loses virulence by simple drying. A cord dried for four days is less virulent than one that has been dried for three, and more virulent than one dried for five. A cord dried for a fortnight has lost all virulence: even a large dose of it will not produce the disease. By this method of drying, Pasteur was enabled to obtain the virus in all degrees of activity: he could always keep going one or more series of cords, of known and exactly graduated strengths, according to the length of time they had been dried—ranging from absolute non-virulence through every shade of virulence.

And, as with fowl-cholera and anthrax, so with rabies; a virus which has been attenuated till it has been rendered innocuous, can yet confer immunity against its more virulent forms: just as vaccination can protect against small-pox. A man, bitten by a rabid animal, has at least some weeks of respite before the disease can break out; and, during that time of respite, he can be immunised against the disease, while it is still dormant: he begins with a dose of virus attenuated past all power of doing harm, and advances day by day to more active doses, guarded each day by the dose of the day before, till he has manufactured within himself enough antitoxin to make him proof against any outbreak of the disease.

The cords used for treatment are removed from the bodies of the rabbits, by an aseptic method, and are cut into lengths and hung in glass jars, with some chloride of calcium in them, for drying. The jars are dated, and then kept in glass cases in a dark room at a constant temperature. To make sure that the cords are aseptic, a small portion of each cord is sown on nutrient jelly in a test-tube, and watched, to see that no bacteria occur in the tube. For each injection a certain small quantity of cord is rubbed-up in sterilised fluid ; and these subcutaneous injections give no pain or malaise worth considering.

Of course, the treatment is adjusted to the gravity of the case. A bite through naked skin is more grave than a bite through clothing ; and bites on the head or face, and wolf-bites, are worst of all. The number and character of the scars are also taken into account. An excellent description of the treatment, by a patient, was published in the *Birmingham Medical Review* of January, 1898. It gives the following tables of treatment :—

1. *Ordinary Treatment.*

Day of Treatment.		Days of Drying of Cord.
1	.. ..	14 and 13
2	.. ..	12 and 11
3	.. ..	10 and 9
4	.. ..	8 and 7
5	.. ..	6
6	.. ..	6
7	.. ..	5
8	.. ..	4
9	.. (½ dose)	3
10	.. (full dose)	5
11	.. ..	5
12	.. ..	4
13	.. ..	4
14	.. (½ dose)	3
15	.. (full dose)	3

2. *Cases of Moderate Gravity.*

Same treatment, up to 13th day.

Day of Treatment.		Days of Drying of Cord.
14	.. ..	3
15	.. ..	5
16	.. ..	4
17	.. (½ dose)	3
18	.. (full dose)	3

3. *Grave Cases.*

Same treatment, up to 10th day.

Day of Treatment.		Days of Drying of Cord.
11	.. ..	4
12	.. ..	3
13	.. ..	5
14	.. ..	5
15	.. ..	4
16	.. ..	4
17	.. (½ dose)	3
18	.. (full dose)	3
19	.. ..	5
20	.. ..	3
21	.. ..	4
22	.. ..	3

4. *Very Grave Cases.*

Same treatment as 3, and in addition

Day of Treatment.		Days of Drying of Cord.
23	.. ..	5
24	.. ..	4
25	.. (½ dose)	3
26	.. (full dose)	3

Furious criticism, unbelief, and flagrant misstatement of facts began at once, and lasted more than two years. Of Pasteur's opponents, the chief was M. Peter, who besought the Académie des Sciences, about once a week, that they should close Pasteur's laboratory, because he was not preventing hydrophobia but producing it. But it does not matter what was said fourteen years ago. In this country, the Report of the 1886 Committee, and the Mansion House meeting in July, 1889, mark the decline and fall of all intelligent opposition to the work. Among so many thousand cases, during so many years, it would be a miracle indeed if not a single case had failed or gone amiss; but we are concerned here with the thousands. Take only the four latest reports, from Athens, Palermo, Rio, and Paris. It is to be noted that the patients, alike at Paris and at other Institutes, are divided into three classes:—

"A. Bitten by animals proved to have been rabid by the development of rabies in other animals inoculated from them.

"B. Bitten by animals proved to have been rabid by dissection of their bodies by veterinary surgeons.

"C. Bitten by animals suspected to have been rabid."

It is to be noted also, as a fact proved beyond doubt, that the full benefit of the treatment is not obtained at once; the highest degree of immunity is reached about a fortnight after the discontinuance of the treatment. Those few cases, therefore, where hydrophobia has occurred, not only in spite of treatment, but within a fortnight of the last day of treatment, are counted as cases where the treatment came too late.

Finally, what was the risk of a bite from a rabid animal, in the days before 1885? It is a matter of guess-work. One writer, and one only, guessed it at 5 per cent; another guessed it at 55, and a third came to the safe conclusion that it was "somewhere between these limits." Leblanc, who is probably the best guide, put it at 16; and Pasteur himself put it between 15 and 20. But suppose it were only 10; that, before Pasteur, out of every 100 men bitten by rabid animals, 90 would escape and only 10 would die of hydrophobia; then take this fact, that in one year, at one Institute alone, there were 142 patients treated, bitten by animals that were proved, by the unanswerable test of inoculation, to have been rabid; and 1 death. And every year the same thing; and in all the 12 years together 2,872 such cases and 20 deaths—a mortality not of 10 per cent., but of less than 1 per cent.

1. Athens.

The *Annales de l'Institut Pasteur*, June, 1898, contain Dr. Pampoukis' report of three years' work at the Hellenic Institute, from August, 1894, to December, 1897. During this period 797 cases were treated—590 male and 207 female. The animals that bit them were—dogs, 732; cats, 34; wolf, 1; other animals, 13; and the 17 other patients had been exposed to infection from the saliva of hydrophobic patients. Of the 797 cases, 245 were of class A, 112 B, and 440 C.

"Among the 797 persons treated, there are two deaths, one in class B and the other in class C. Thus the mortality has been 0·25 per cent. Besides these two who died of rabies there are five more, in whom the first signs of rabies showed themselves in less than fifteen days after the last inoculation.

"Finally, beside these 797 cases, there is one other case, bitten by a wolf, in whom the treatment failed. If we reckon this last case in the statistics of mortality, we have three deaths in 798 cases = 0·37 per cent.

"Beside these 798 cases treated at the Institute, there have been others that have not undergone the antirabic treatment, having trusted the assurances of those who are called in Greece *empirics*. Among these non-treated cases there are 40 who have died of rabies."

2. PALERMO.

The *Annales* for April, 1896, give the report by Dr. de Blasi and Dr. Russo-Travali of the work of the Municipal Institute at Palermo, during 8½ years, from March, 1887, to December, 1895. The number of cases was 2,221; in 1,240 (class A), the animals were proved to have been rabid by the result of inoculations; in 981, there was reason to suspect rabies.

"Setting aside five patients who died during the course of the treatment, and five others who died less than fifteen days after the end of the treatment, we have had to deplore only nine failures = 0·4 per cent. Even if we count against ourselves the ten other cases, the mortality is still only 0·85."

3. RIO DE JANEIRO.

The *Annales* for August, 1898, give Dr. Ferreira's report of ten years' work (February, 1888–April, 1898) at the Pasteur Institute at Rio. The number of cases treated was 2,647, of whom 1,987 were male and 660 female. Beside these 2,647 there were 1,234 who were not treated, because it was ascertained that they were in no danger of rabies; 3 who were brought to the Institute, already suffering from the disease; and 59 who refused treatment.

Of the 2,647 persons treated, 10 had pricked their hands at work in the laboratory, 3 had exposed chance scratches on their hands to the saliva of rabid animals, and 1 had been bitten by a rabid patient. Of the rest, 1,886 had been bitten on the bare skin, and 747 through clothing.

In 236 cases the rabies of the animal had been proved by inoculation. In 1,173 it had been recognised by the signs of the disease. In 1,238 there was good reason to suspect that the animal had been rabid.

Of the 2,647 patients, in 30 cases the treatment was stopped, because the animals were at last traced, after treatment was begun, and were found not to be rabid. In 65 cases the patients, after treatment was begun, refused to go on with it, and 3 of them died of rabies. In 6 cases rabies developed during treatment; 5 of them had been very badly bitten about the head, and 1 did not come for treatment till the twenty-first day after the bite, and was attacked by rabies two days later. And 5 cases died of other maladies that had nothing to do with rabies. Setting aside these 106 cases, there remain 2,541 cases, with 20 deaths = 0·78 per cent. But, of these 20 deaths, 9 occurred within fifteen days of the end of treatment, before protection was fully established. If these 9 deaths be excluded, the figures stand at 2,532 cases, with 11 deaths = 0·43 per cent.

4. PARIS.

Dr. Pottevin's report on the work of the Pasteur Institute (*Annales*, April, 1898) must be given word for word, without abbreviation.

EXPERIMENTS ON ANIMALS

I.

During 1897, 1,521 patients received the antirabic treatment at the Pasteur Institute: 8 died of rabies. The notes of their cases will be found at the end of this paper.

If we exclude 2 of these 8 cases—the cases of Heniquet and Morin, where death occurred before it was possible for the vaccinations to produce their effect—the results of the vaccinations in 1897 are—

Patients treated	1,519
Deaths	6
Mortality per cent.	0·39

In the following table these figures are compared with those of preceding years :—

Year.	Patients treated.	Deaths.	Mortality per cent.
1886	2,671	25	0·94
1887	1,770	14	0·79
1888	1,622	9	0·55
1889	1,830	7	0·38
1890	1,540	5	0·32
1891	1,559	4	0·25
1892	1,790	4	0·22
1893	1,648	6	0·36
1894	1,387	7	0·50
1895	1,520	5	0·33
1896	1,308	4	0·30
1897	1,521	6	0·39

RABIES

II.

Patients treated at the Pasteur Institute are divided into three classes as follows :—

A. The rabies of the animal was proved by experiment, by the development of rabies in animals inoculated with its bulb (the upper end of the spinal cord).[1]

B. The rabies of the animal was proved by veterinary examination (dissection of its body).

C. The animal was suspected of rabies.

We give here the patients treated in 1897, under these three classes :—

	BITES OF THE HEAD.			BITES OF THE HANDS.			BITES OF THE LIMBS.			TOTAL.		
	Patients.	Deaths.	Mortality p. c.	Patients.	Deaths.	Mortality p. c.	Patients.	Deaths.	Mortality p. c.	Patients.	Deaths.	Mortality p. c.
A	15	0	0	81	0	0	46	1	2·1	142	1	0·7
B	106	0	0	539	4	0·74	273	1	0·4	918	5	0·65
C	30	0	0	244	0	0	187	0	0	461	0	0
	151	0	0	864	4	0·46	506	2	0·4	1,521	6	0·39

The following tables, giving the results obtained since the vaccinations were first used, show that the gravity of the bites varies with their position on the body, and that the mortality is always below 1 per cent. among patients bitten by dogs undoubtedly rabid :

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[1] It is satisfactory to know that rabbits affected with rabies do not suffer in the same way as dogs and some other animals, but become subject to a painless kind of paralysis.

	Patients.	Deaths.	Mortality.
Bites of the Head ..	1,759	21	1·1
Bites of the Hands ..	11,118	53	0·47
Bites of the Limbs ..	7,289	22	0·30
	20,166	96	0·46

	Patients.	Deaths.	Mortality.
A ..	2,872	20	0·69
B ..	12,547	61	0·48
C ..	4,747	15	0·31
	20,166	96	0·46

III.

In regard to their nationality, the 1,521 patients treated at the Pasteur Institute in 1897 were as follows :—

Germany ...	8	United States ...	1
England ...	83	Greece ...	1
Belgium ...	14	India	33
Egypt... ...	2	Switzerland ...	33

That is, 175 foreigners and 1,346 French.

IV.

Notes of the eight cases where the treatment failed :—

1. Camille Bourg, 26. Bitten April 11th ; treated at the Pasteur Institute April 13th to 30th ; died of rabies at the Lariboisière Hospital, May 26th. Six penetrating bites on the ball of the left thumb. The dog was examined by M. Grenot, a veterinary surgeon at Paris, and the dis-

section gave evidence of rabies. Another person bitten and treated at the same time as Bourg is now in good health.

2. Louis Fiquet, 23. Bitten April 22nd; treated at the Pasteur Institute, April 23rd–May 10th; died of rabies at the Necker Hospital, June 4th. Five bites, two of them deep, round the right thumb. They had been cauterised five hours after infliction. The dog was examined by M. Caussé, a veterinary surgeon at Boulogne, and the dissection gave evidence of rabies. Another person bitten at the same time as Fiquet is now in good health.

3. Annette Beaufort, 19. Licked on the hands, which were chapped, on April 15th. The dog was killed next day, examined, and declared to have been rabid by M. Lachmann, a veterinary surgeon at Saint-Etienne. Treated at the Pasteur Institute, April 20th–May 7th. Died of rabies October 14th. Two other persons bitten by the same dog and treated at the Pasteur Institute are now in good health.

4. Julien Heniquet, 53. Bitten March 11th by a dog that M. Jenvresse, veterinary surgeon at Beaumont-sur-Oise, declared after dissection to have been rabid. One bite had torn the lower lip, the wound had been sutured; three other wounds on the nose. The wounds had not been cauterised. Treated at the Pasteur Institute, May 18th–June 5th. First symptoms of rabies showed themselves June 4th, before the treatment was finished; died June 7th. As the disease had its onset during the course of the inoculations, this case should be excluded from the number of those who died of rabies after treatment.

5. Germain Segond, 7. Penetrating bite on the bare right fore-arm, May 23rd. Cauterised an hour later with a red-hot iron. Treated May 26th–June 9th; died of rabies July 22nd. The dog's bulb had been sent to the

Pasteur Institute. A guinea-pig inoculated in the eye May 26th was seized with rabies September 10th.

6. Suzanne Richard, 8. Bitten June 12th on the left leg by a dog, found on dissection to have been rabid by M. Touret, veterinary surgeon at Sannois. The bite, penetrating 3 cm. long, had been sutured; it had been made through a cotton stocking, and had been cauterised in half an hour. Treated June 13th–30th; died of rabies August 2nd. (Notes from M. le Dr. Margny, at Sannois.)

7. Joseph Vaudale, 33. Bitten on the left hand, August 8th. Six penetrating bites on the back of the hand; had not been cauterised. The dog was declared rabid by M. Verraert, veterinary surgeon at Ostend. Treated at the Pasteur Institute, August 11th–28th; died of rabies September 27th.

8. Paul Morin, 38. Bitten August 24th on the left cheek, a single bite, 2 cm. long; no cauterisation. The dog was sent to the Alfort School, August 25th, and found to be rabid. Treated at the Pasteur Institute August 26th–September 15th. Died of rabies some days after the end of treatment (three weeks after the bite, says a note sent to us). The interval between the end of the treatment and the onset of the disease being less than fourteen days, Morin must not be counted in the number of patients inoculated under conditions which permit successful inoculation.

It is not impossible that some sort of intensive modification of Pasteur's treatment may be found not for the prevention, but for the cure of hydrophobia; and two successful cases of this kind have been reported in the *Annales*. Apart from this faint hope, the cure of hydrophobia is where it was in the days of the "Tonquin medicine" and the "Tanjore pills." As for the "Buisson Bath Treatment for the Prevention and Cure of Hydrophobia," it failed egregiously to afford the very least benefit to inoculated animals, and the evidence in its favour is just like the evidence for Mother Siegel's Syrup. Dr. Buisson himself thought he had hydrophobia, and took a vapour-bath to kill himself: *and at* 42 *degrees* (127 *Fahrenheit*) *I was cured.* It was an ordinary case of fear of hydrophobia. Then there is "a mass of cures effected in Asia": we know that mass of cures in Asia: but only one of them is quoted, and in that case nothing is said about the dog. Finally, there is the case of Pauline Kiehl, who was "refused treatment by M. Pasteur," which is certainly the strangest feature of the case: but it is not said where this case is published. The whole thing is arrant nonsense.[1]

NOTE.

The *Annales* for June of this year contain the 1898 report from the Pasteur Institute. The number of patients treated was 1,465, of whom 4 died of rabies, but one of them died only ten days after treatment.[1] Two patients were seized by rabies during treatment, and are not counted among those treated. The figures therefore are—

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[1] The latest report of the "Buisson treatment" (*Abolitionist*, August 15, 1899) is wonderful. A native of Dacca writes—"No fewer than thirty cases we treated successfully. One case bitten by a cobra we treated with wonderful success, and another by a rabid fox." It does not say whether the cobra was rabid. Another case is reported by a lady doctor, "Physician in charge of the Temperance and Buisson Institute, No. 2, Clare Road, Byculla." This was a little boy, bitten by a dog "suspected, though not proved, to be rabid." "If this case be interpreted as one of Tetanus rather than Hydrophobia, it only indicates another important use for the Buisson bath." *Interpreted* is good: and the Indian Government ought to note that this idiotic bath is used alike for rabies, snake-bite, and (?) tetanus.

Cases treated	1,465
Deaths	3
Mortality	0·2 per cent.

	Bites on the Head.			Bites on the Hands.			Bites on the Limbs.			Total.		
	Treated.	Died.	Mortality.	Treated.	Died.	Mortality.	Treated.	Died.	Mortality.	Treated.	Died.	Mortality.
Table A	11	0	0	100	0	0	30	0	0	141	0	0
Table B	80	0	0	549	1	0·18	226	0	0	855	1	0·11
Table C[1]	41	0	0	265	1	0·37	163	1	0·61	469	2	0·42
Total	132	0	0	914	2	0·22	419	1	0·24	1465	3	0·20

[1] A. La rage de l'animal mordeur a été expérimentalement constatée par le développement de la maladie chez des animaux mordus par lui ou inoculés avec son bulbe.

B. La rage de l'animal mordeur a été constatée par examen vétérinaire.

C. L'animal mordeur est suspect de rage.

Of the three patients who died more than fifteen days after the treatment, one came from India

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[1] "D'après les expériences faites sur les chiens, on est autorisé à penser que les centres nerveux des personnes mortes de rage dans les 15 jours qui suivent le traitement ont été envahis par le virus rabique avant que la cure ait pu avoir toute son efficacité."

(Lahore), bitten August 22nd, treated in Paris September 12th–October 26th, died in India November 23rd. "Son cas a donné lieu à certaines polémiques. Un journal anglais des Indes, *The Englishman*, a publié une dépêche d'après laquelle le chien qui avait mordu O'Leary serait encore vivant et en parfaite santé ; ce fait nous a été signalé par un rapport de M. le consul général de France à Calcutta, que M. le ministre des Affaires étrangères a bien voulu nous communiquer ; nous avons procédé à une enquête, et nous donnons ci-dessous un extrait d'une lettre qui nous a été addressée des Indes le 20 avril par le frère de O'Leary ; il met les choses au point, 'Vous me demandez des renseignements sur le chien qui a mordu mon frère, on n'a pas retrouvé sa trace et aucun vétérinaire n'a pu l'examiner ; à part mon pauvre frère, personne n'a vu ce chien, on n'a donc aucune preuve qu'il fût malade ; mais en même temps que mon frère, il a mordu un petit chien à nous, celui-ci était encore vivant quand mon frère est mort, depuis on l'a abattu.'"

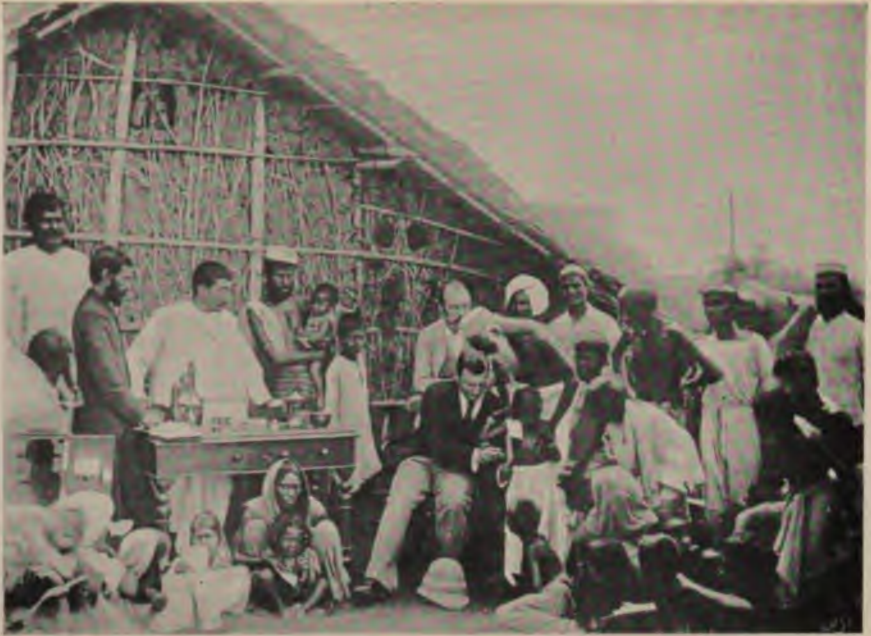
Of the two patients who died during treatment, one was a street-singer, bitten in thirteen places on the face and hands : "trois autres personnes mordues par le même chien et traitées à l'Institut Pasteur sont actuellement en parfaite santé." The other was a child three years old, from Castleblarney, bitten on the face. The patient who died only ten days after treatment was this child's brother, seven years old, bitten on the face, arm, and hand.

VIII

CHOLERA

THE study of cholera was the hardest of all the hard labours of bacteriology; it took years of work in all parts of the world, and the difficulty and disappointments over it are past all telling. Koch's discovery of the "comma-bacillus" (1883) raised a thousand questions that were solved only by infinite patience, international unity for science, and incessant research; and the Hamburg epidemic (1892) marks the time when the comma-bacillus was at last recognised as the cause of cholera. A mere list of the men who did the work would fill page after page here; it was bacteriology *in excelsis*, often dangerous, and always laborious.

There is the same heroic note in the story of the preventive treatment of cholera by Haffkine's method; one of the men in whom Pasteur seems to live again. He began in 1889, under Pasteur's guidance, to study the immunisation of animals against the cholera-



Haffkine's first preventive inoculations against Cholera in a Calcutta bustee, March, 1894.

bacillus. Other men, of course, were working on the same lines — Pfeiffer, Brieger, Metchnikoff, Fischer, Gamaleïa, Klein, Wassermann, and many more— and by 1892 the immunisation of animals was proved up to the hilt. Then came the advance from animals to men, from laboratories to Indian cities, villages, and cantonments; and here the honour is Haffkine's, and his alone. Ferran's inoculations (Spain, 1885) had failed. Haffkine, having tested his method on himself and his friends, went to India, with a commendatory letter from our Government :—

> "Researches on cholera, with special reference to inoculation, were undertaken and carried on in my laboratory, in the Pasteur Institute in Paris, between 1889 and 1893. The experiments resulted in the elaboration of the present method, which when tried on animals was found to render them resistant against every form of cholera-poisoning otherwise fatal to them.
>
> "The physiological and pathological effect on man was then studied on some sixty persons, mostly medical and scientific men interested in the solution of the problem. The effect was found to be harmless to health. The next step was to transfer the operations to the East." (Haffkine's *Report to the Government of India*, 1895.)

He reached Calcutta in March, 1893, and at the request of Mr. Hankin[1] was invited to Agra; here, in April, he vaccinated over 900 persons, including many English officers. From Agra to Aligarh; and from Aligarh he was asked to more places than he could visit. In 1895 his health failed, and no wonder; and he came back to Europe for a short time:—

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[1] Mr. Hankin, whose name is had in remembrance by Cambridge men, is Chemical Examiner and Bacteriologist to the North-West Provinces and Oudh, and to the Central Provinces.

> "My actual work in India lasted twenty-nine months, between the beginning of April, 1893, and the end of July, 1895. During this period the anti-cholera vaccination has been applied to 294 British officers, 3,206 British soldiers, 6,629 native soldiers, 869 civil Europeans, 125 Eurasians, and 31,056 natives of India. The inoculated people belonged to 98 localities in the North-West Provinces and Oudh, in the Punjab, in Lower Bengal and Behar, in the Brahmaputra valley, and in Lower Assam. No official pressure has been brought on the population, and only those have been vaccinated who could be induced to do so by free persuasion. In every locality, efforts were made to apply the operation on parts of large bodies of people living together under identical conditions, in order to compare their resistance in outbreaks of cholera with that of non-inoculated people belonging to the same unit of population. This object has been obtained in 64 British and native regiments, in 9 gaols, in 45 tea-estates, in the fixed agricultural population of the villages parallel to Hardwâr pilgrim road, in the *bustees* of Calcutta, in a certain number of boarding-schools, where the parents agreed to the inoculation of their children, in orphanages, &c. The vast majority of inoculated people lived thus under direct observation of the sanitary and medical authorities of India." (Haffkine, Lecture in London. *British Medical Journal*, Dec. 21, 1895.)

Altogether, upwards of 70,000 injections on 42,179 people—*without having to record a single instance of mishap or accident of any description produced by our vaccines.* Consider the colossal difficulties of this new treatment: the frequent running short of the vaccine, preventing a second injection; the absolute necessity, at first, of using very small doses of a weak vaccine, lest one disaster should occur; the impossibility of avoiding, now and again, some loss of strength in the vaccine; the impossibility of knowing how long the protection would last. Surely in all science there is nothing to beat this first voyage of adventure single-handed to fight the cholera in India.

Later than Haffkine's 1895 report, we have Dr. Simpson's 1896 report: "*Two Years of Anti-choleraic Inoculations in Calcutta.* By W. J. Simpson, M.D., M.R.C.P., D.P.H., Health Officer, Calcutta." The date of this report is July 8, 1896; and it gives not only the Calcutta results, but all that are of any use for exact judgment[1]:—

> "The results of Calcutta are fully confirmed by those obtained in other parts of India, wherever it was possible to make all the necessary observations with precision, and wherever the cases were sufficiently numerous to show the effect of the inoculation.
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> "Outside Calcutta, since the commencement of the in-

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[1] For a summary of this report see the *Lancet*, August 8, 1896. For more recent results, see Surgeon-Captain Vaughan and Assistant-Surgeon Mukerji, in the thirtieth annual report of the Sanitary Commissioner for Bengal (1897). Also the cases published by Surgeon-Captain Nott, in the *Indian Medical Gazette*, May, 1898.

oculations in India in April, 1893, opportunities for an exact comparison of the respective powers of resistance against cholera of inoculated and non-inoculated persons presented themselves : (1) in Lucknow, in the East Lancashire Regiment, (2) in Gaya, in the jail, (3) in Cachar, among the tea-garden coolies, (4) in Margherita, among coolies of the Assam-Burmah Railway Survey, (5) in Durbhanga, in the jail, (6) in the coolie camp at Bilaspur, (7) in Serampur among the general population."

Here, then, in this 1896 report, are all the results that give an answer to the question, What will happen when cholera breaks out among a number of people living under the same conditions, of whom some have received preventive treatment, and the rest have been left to Nature ?

1. Calcutta (1894–1896).

"The number of people inoculated during the period under review was 7,690 ; of these, 5,853 are Hindus, 1,476 Mahomedans, and 361 other classes. . . . Considering that the system is a new one, that the inoculations are purely voluntary, and everything connected with them has to be explained before the confidence of the people can be obtained, and considering how long new ideas are in taking root among the general population—and in this case it is not merely the acceptance of an idea, but such faith in it as to consent to submit to an operation—the number is certainly satisfactory for a beginning. The present problem can be compared with the introduction of vaccination against small-pox into Calcutta. It took 25 years before the number of vaccinations reached an average of 2,000 ; whereas the inoculations against cholera have in two years nearly doubled that average. This is a proof that in spite of the difficulties, which every new movement naturally has to meet with, there are large numbers of people anxious to avail themselves of the protective effect of the inoculations.

"Although all sorts and conditions of individuals, weak and strong, sickly and healthy, young and old, well-nourished and badly nourished, and often persons suffering from chronic diseases, have been inoculated, in every instance, without exception, the inoculations have proved perfectly harmless.

"The investigations on the effect of the inoculation are made exclusively in those houses in which cholera has actually occurred, the object being to ascertain and compare the incidence of cholera on the inoculated and not inoculated in those houses in which inoculations had been previously carried out. *For this purpose, affected houses in which inoculations have not been performed, and inoculated houses in which cholera has not appeared, are excluded.*"

Nature gave a demonstration in 77 houses. In one house, and one only, all the household had been inoculated; in 76, inoculated and non-inoculated were living together; but of these 76 houses, 6 are excluded from the table of results, because the inoculated in them were so few—less than one-tenth of the household—that their escape from cholera might be called chance. The cholera came, and left behind it this fact:—

654 uninoculated individuals had 71 deaths
=10·86 per cent.
402 inoculated in the same households had
12 deaths = 2·99 per cent.

If we add the 6 houses that Dr. Simpson excludes, we find that in 77 houses there were 89 deaths from cholera; 77 being among the uninoculated, and 12 among the inoculated.

Moreover, of these 12 deaths, 5 occurred during the first five days after inoculation—that is to say, during the period in which the protective influence of the vaccine was still incomplete. *Then came a period of more than a year, during which the uninoculated had 42 deaths, and the inoculated had one death.* The remaining 6 of the 12 deaths occurred more than a year after inoculation; and 5 of these 6 had received only one inoculation of the weak vaccine that was used early in 1894.

Take a good instance that came at the very beginning of the work:—

> "A local epidemic took place around two tanks in Kattal Began *bustee*, ward 19, occupied by about 200 people. In this *bustee*, about the end of March, two fatal cases of cholera, and two cases of choleraic diarrhœa, occurred. The outbreak led to the inoculation of 116 persons in the *bustee* out of the 200. Since then, 9 cases of cholera, of which 7 were fatal, and one case of choleraic diarrhœa have appeared in the *bustee*, and it is a very extraordinary fact that all these 10 cases of cholera have occurred exclusively among the uninoculated portion of the inhabitants, which, as stated, forms the minority in the *bustee;* while none of the inoculated have been affected." ("*Cholera in Calcutta in* 1894." W. J. Simpson.)

CHOLERA

2. LUCKNOW (1893).

The story of the outbreak of cholera in the East Lancashire Regiment must be read carefully :—

> "Rumour magnified the events connected with this outbreak, and distorted the facts connected with the inoculations; and as a result, the current of public opinion, which had previously been in favour of inoculation, set in strongly in the opposite direction. The advocates of anti-choleraic inoculations were abused in no particularly measured terms, and the inoculations were held up to be the source of every possible evil and danger . . . of the most loathsome diseases, and of every ill which man is heir to. The distrust engendered by these misrepresentations and fulminations was, however, only of a temporary nature; and when the exact circumstances came to be known and understood, the confidence created by the Calcutta experience began to be considerably restored. Inoculations were performed in May, 1893, in the East Lancashire, Royal Irish, 16th Lancers, 7th Bengal Infantry, 7th Bengal Cavalry, and general population in the Civil Lines. In 1894, cholera appeared among the native population of Lucknow, in the form of an epidemic distinguished by its extreme virulence, patients succumbing in the course of a few hours. It is stated that the epidemic was of a most malignant type. In the latter part of July it entered the cantonments, and attacked the East Lancashire, almost exclusively confining its ravages to that regiment."

In the East Lancashire, 185 men were inoculated in May, 1893. From the statistical returns obtained from the military authorities at Lucknow, it appears that at the time of the outbreak, in July, 1894, the strength of the men, including those in hospital, was 773; and, of these, 133 had been inoculated, as recorded in the inoculation register, and 640 had not been inoculated.

The following table shows the total number of attacks and deaths in not-inoculated and inoculated:—

		Attacks.	Deaths.
Non-inoculated	640 ...	120=18·75	79=12·34 p. c.
Inoculated ...	133 ...	18=13·53	13= 9·7 p. c.

The men were moved into camp; but this movement seemed only to make things worse: "the epidemic in the camp appears to have been twice as severe as in the cantonment."[1]

Lucknow came so early in the work of inoculation, that weak vaccines were used in small doses. The cholera, when it broke out, was "of a most malignant type, senior medical officers of long experience in the country stating that such a virulent cholera had not been seen by them for very many years past." More than a year had elapsed between the inoculations and the outbreak of the cholera. It is no wonder that the regiment was not well protected:—

> "The small amount of protection which the inoculations afforded in this case may have depended on the

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[1] "The moving into camp, notwithstanding this example, is all the same an excellent measure of defence, and would with reason be adopted in every outbreak." (Simpson, *loc. cit.*)

> mild effects which the injections produced on the men, at the time of the operation in 1893, in comparison with the severity of the epidemic which attacked the regiment. It is recorded in the Lucknow Inoculation Registers that only in two men, out of the 185 inoculated in 1893, a marked febrile reaction was obtained ; in 77 individuals the vaccinal fever was only slight, while in 66 there was no reaction : an effect which was due to the weakness of the vaccines procurable at that period of work, and to the small doses used. The influence of the vaccines was possibly further reduced, at the time of the epidemic, by a lapse of fourteen to fifteen months." (Haffkine, 1895 Report.)

3. Gaya Jail.

4. Assam-Burmah Railway.

On July 9, 1894, an outbreak of cholera occurred in the Gaya jail, and by June 18th there had been 6 cases and 5 deaths. On that day and the next day, 215 prisoners were inoculated. The average number of the prisoners, during the outbreak, was 207 inoculated and 202 not inoculated. Surgeon-Major Macrae, superintendent of the jail, reports :—

> "The inoculations being purely voluntary, no selection of prisoners was possible, but all classes of the jail were represented—male and female, old and young, habituals and less frequent offenders, strong and weakly, convalescent and even hospital patients sent their representatives ; no difference of any kind was made between inoculated and non-inoculated ; they were under absolutely identical conditions as regards food, water, accommodation, &c., in fact in every possible respect."

Of course, the best results could hardly be obtained, because the cholera was already at work: it took about ten days for the 1894 vaccine to produce its full effect; and two inoculations were generally made, one five days after the other. This gradual action of the vaccine is well shown in Dr. Simpson's table:—

	NON-INOCULATED, 202.		INOCULATED, 207.	
	Cases.	*Deaths.*	*Cases.*	*Deaths.*
During 5 days after 1st inoculation	7	5	5	4
During 3 days after 2nd inoculation	5	3	3	1
After 3 days after 2nd inoculation	8	2	0	0
Total...	20	10	8	5

Haffkine's comment on these figures must be noted here:—

"In the Gaya jail, the inoculations were *for the first time* applied *in a prevalent epidemic*, and *very weak doses* of a relatively weak vaccine were used. . . . Far higher results have been obtained by an application of stronger doses. In the *bustees* situated round the tanks in Calcutta, where cholera exists in a permanent state, the disease occurred in 36 houses with inoculated people. In each of these houses there was one part of the family inoculated and another not. The observations were continued for 459 days, with the following results:—

During the first period of 5 days subsequent to the inoculation with 1st vaccine, cholera occurred in 8 houses.

75 non-inoculated had 5 cases, with 3 deaths.
52 inoculated had 3 cases, with 3 deaths.

During the second period, of 5 days subsequent to the 2nd inoculation, cholera occurred in 2 houses.

8 non-inoculated had 2 cases, with 2 deaths.
17 inoculated had 0 cases.

After the 10 *days necessary for the preventive treatment had expired, and up to the* 459*th day, the disease visited* 26 *houses.*

263 *non-inoculated had* 38 *cases, with* 34 *deaths.*
137 *inoculated had* 1 *case, with* 1 *death, in a child that had not been brought up for the second inoculation.*"

And, for a good instance of lives saved even during an outbreak, take the Assam - Burmah Railway coolies :—

"Three hundred and fifty[1] Khassia Hill coolies had been collected for the survey party of the Assam-Burmah Railway, and put under the escort of a detachment of Goorkhas, when cholera broke out amongst them. The largest part of the coolies immediately submitted to the preventive inoculation, the rest remained uninoculated. The result was that *among the not-inoculated minority there were* 34 *cases, with* 30 *deaths; whereas the inoculated had* 4 *fatal cases.*" (Haffkine, 1895, *Lecture in London*).

5. DARBANGHA JAIL (1896).

The figures in this instance are small: but Surgeon-Captain E. Harold Brown's report is very pleasant reading. Cholera broke out in the jail on March 31, 1896, and by April 9th there had been eight cases. Next day, 172 prisoners were moved into camp twelve miles away; and 53 were left behind, the sick in the jail hospital, the patients in the cholera huts, with their attendants, the old and infirm, and a few cooks and sweepers. That day, three cases occurred in the camp, and one in the jail; and on the 11th, at 2 and 4 a.m., two more cases were reported in camp. At 7.30 a.m., Haffkine and Dr. Green came to the camp:—

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[1] The exact number is 355, of whom 196 were inoculated: the coolies numbered 343, and the Goorkha sepoys 12. See Dr. Simpson's 1896 Report.

> "The prisoners were spoken to on the subject, and seemed to be pleased with the idea, the word *tika* (inoculation), which was familiar to them from its association with small-pox, appearing to appeal to them. They were accordingly arranged in four rows facing the tent, in front of which Dr. Haffkine was about to commence operations. I was the first subject to be inoculated; and after me the jailor, assistant jailor, hospital assistant and three warders. The first prisoner in the front rank was next brought up and submitted cheerfully; after which, every alternate man was taken, so that no selection of cases was made, until one half of the total number were inoculated. Those who had not been inoculated were far from pleased at having been passed over; and, to our surprise, they rose almost to a man, and begged to be inoculated; nor were they satisfied when told that the medicine was exhausted."

The dose administered on this occasion (April 11, 1896) was stronger than the Gaya jail dose (July 18, 1894): it acted in a few hours, and the reaction was well marked.

"There were fresh cases of cholera that day at 12 (noon), 6, 6, 7, and 7.30 p.m., and at midnight, all in those who had not been inoculated, and all terminating fatally, despite the greatest care and the most prompt and assiduous treatment. On the 12th two further cases occurred, both among the uninoculated, and both died; there being thus eight cases in succession, all from the men who were not inoculated, and all proving fatal."

The inoculations were made at 7.30 a.m. Surgeon-Captain Brown had pain within half an hour, and fever in three hours, with temperature 104°, *but this was probably due to the fact that I was not able to rest.* The prisoners, of course, went to bed: they all reacted before 4 p.m., but did not have so much trouble over it. The last case was on the 15th. The outbreak was a bad type of cholera; out of 30 cases 24 died, some of them in 1½–4 hours. "To summarise the combined results of the camp and the jail, we find that of a daily average of 99 non-inoculated there were 11 cases, all fatal, = 11·11 per cent.; of 110 inoculated there were 5 cases, with 3 deaths = 2·73 per cent." One of these five deaths was the case of an old infirm prisoner, who before being attacked with cholera had suffered for thirty hours with diarrhœa.

6. BILASPUR AND SERAMPUR.

Here again the figures are small, but worth noting. In a coolie camp at Bilaspur (Central Provinces) 100 non-inoculated had 5 deaths, and 150 inoculated had 1 death. In Serampur, among the general population, 51 non-inoculated had 5 cases and 3 deaths, and 42 inoculated had 2 cases and 1 death.

7. The Cachar Tea-Gardens (1895).

This series of inoculations was begun in February, 1895, for the protection of the coolies on various tea-estates. The results are excellent, and deal with large numbers.[1] The latest report from Dr. Arthur Powell, the Medical Officer, is quoted in Dr. Simpson's 1896 report :—

At Kalain—
 1,079 not inoculated had 50 cases, with 30 deaths.
 1,250 inoculated—3 cases, with 2 deaths.[2]
At Kalaincherra—
 685 not inoculated had 10 cases, with 7 deaths.
 155 inoculated—no cases.
At Degubber—
 254 not inoculated had 12 cases, with 10 deaths.
 407 inoculated—5 cases, all recovered.
At Duna—
 121 not inoculated had 4 cases, with 2 deaths.
 29 inoculated—no cases.
At Sandura—
 454 not inoculated had 2 cases, with 1 death.
 51 inoculated—2 cases, with 1 death.

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[1] "As a field for testing the value of inoculation, the tea factories of India possess many advantages. The labourers being under contract, the after-history of those inoculated is easily followed up. Each morning the adults are paraded for roll-call ; and all sick must attend hospital, where a record is made of their disease and treatment." (Dr. Powell, *Lancet*, July 13, 1896.)

[2] "It is unfortunate that neither of the fatal cases among the inoculated was seen by any medical man, not even an unqualified Doctor Babu." Dr. Powell does not think, from what was told him, that one of them was cholera.

At Karkuri—

198 not inoculated had 15 cases, with 9 deaths.
443 inoculated—3 cases, with 1 death.

At Craig Park—

185 not inoculated had 1 fatal case.
46 inoculated had no case.

TOTAL.

Not inoculated, 2,976, with 94 cases and 60 deaths.
Inoculated, 2,381, with 13 cases and 4 deaths.

Men talk about Empire-building, and "Deeds that won the Empire," and they know nothing of the everlasting work that Haffkine and men like him have done for the consolidation of India. Already, in 1896, he was working not at cholera but at plague, and had tested his plague-serum on animals and on himself. Then, in January, 1897, came the outbreak of bubonic plague in the Byculla jail, and the first anti-plague inoculations. To praise Haffkine, prose is not good enough, and the Fourth Eclogue not too good :—

Redeunt Saturnia regna :
Aspice, venturo lætantur ut omnia sæclo—

Or, if it be prose, let it be the Viceroy's speech at Calcutta, March 3rd of this year :—

> "I say this, that if we had come back to you from the West with our medicine in our hand, and with that alone, we should have been justified in our return. For what is this medical science we bring to you? It is no mere

collection of pragmatical experimental rules. It is built on the bed-rock of pure irrefutable science ; it is a boon which is offered to all, rich and poor, Hindu and Mohammedan, woman and man. It lifts the *purdah* without irreverence. So far as I know, it is the only dissolvent which breaks down the barriers of caste without sacrilege."

Another most important result of the discovery of the cholera bacillus is its use in diagnosis. If a case of suspected cholera is landed at a British port, the sanitary authority at once takes steps to ascertain whether the specific microbe is present ; and, according to the answer given by bacteriology, either allows the patient to proceed on his journey, or adopts measures of isolation to prevent the spread of the disease to others. Thus, thanks to our insular position, this dreadful disease has for many years been prevented from invading our population.

IX

PLAGUE

THE *Abolitionist*, in its first number (April, 1899) said that the plague in India "goes on unchecked, and the use of Professor Haffkine's fluid has merely demonstrated the capacity of such cultures to harm, not to heal, the patient."

The use of Haffkine's fluid is not to "heal" the plague, but to prevent it. Take, for instance,[1] the report on the plague in Damaun (Portuguese India) :—

"The daily mortality, from the beginning of March to May 17, 1897, was 30 per diem—a grand total of 2,325 deaths. Of this number, 2,093 were authenticated, in the particular families where they had taken place, by means of a house-to-house inquiry set on foot by Shet Sorabjee (head of the Parsee community). Among the Parsee community, numbering 306 persons, 276 were inoculated twice, and 1 once. *Of these, only* 1 *died*, a woman who had only been inoculated once, and that, as was afterwards seen, subsequently to infection by plague. Thus the total mortality among the inoculated Parsees was only 1 in 277, a percentage of **0·36 PER CENT.** Among the 29 uninoculated there were 4 deaths—a mortality of **13·8 PER CENT.** Among Shet Sorabjee's servants and labourers, numbering 200 in all, *all were inoculated but one. That one was attacked* on May 16th, and died on May 19th; while among the inoculated **1 PERSON**, a child aged 4 years, was attacked and died.

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[1] An abstract of this report will be found in the *Lancet*, December 18, 1897. The report was drawn up by Haffkine and Surgeon-Major Lyons.

"Of other members of the population of Damaun, between March 26th and the end of May, among 6,033 uninoculated there were 1,482 deaths, or **24·6 PER CENT.**; while among 2,197 inoculated there were 36 deaths, or **1·6 PER CENT.** If the inoculated had died in the same ratio as the uninoculated, the number of deaths among them would have been 332 instead of 36. Owing to the extreme demand for lymph, the latter inoculations were much weaker than those done at the commencement of the epidemic, and the difference in favour of the stronger lymph was most marked: for out of 1,924 inoculated with the strong lymph there were 70 cases = 3·6 per cent., with 22 deaths = 1·1 per cent.; case mortality, 31·4 per cent.: out of 270 treated with weak lymph there were 21 cases = 7·8 per cent., with 14 deaths = 5·2 per cent.; case mortality, 66·7 per cent.

"Figures such as these show the extreme value of the preventive treatment, *taken as they are from the course of a most virulent epidemic, and during the highest stage of the outbreak.*"

That is the use of Professor Haffkine's fluid; not "to heal the patient." And these facts of the Damaun report were published in the *Lancet* sixteen months before the *Abolitionist* was started.

Take next, though the figures are small, Haffkine's recent Undhera report, April 10, 1898. It is of especial interest, because the inoculated and the non-inoculated were all packed in one village, and every condition of family life was left untouched :—

> "The inoculations were performed in Undhera on the 12th of February, 1898, with the object of demonstrating to the Baroda authorities the protective effect of the measure. On the above date the population of the village, exclusive of the adjacent suburb, consisted of 950 souls, of whom 47 had been inoculated previously, between the 26th of January and the 2nd of February, 1898, by Dr. C. D. Divanjee, of the Baroda Medical Establishment, and were not inoculated again. All the others, for the purpose of inoculation, were collected in the streets and grouped according to the wards where they resided, family by family. In each household, as nearly as was possible, half the number of the male members, half the number of the females, and half the number of the children, were inoculated. The total number of persons thus inoculated was 466, giving, with the 47 inoculated previously, a total of 513, while 437 remained uninoculated."

The plague in the village lasted up to March 26th, and fell on 28 families. In these, there were 64 not inoculated, and 71 inoculated. The 64 had 27 cases, with 26 deaths ; the 71 had 8 cases, with 3 deaths.[1]

> "If the inoculated had suffered to the same extent as their uninoculated relatives, they would have had, propor-

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[1] In one of these 3 deaths, there was no interval between the fever of reaction and the fever of plague ; the patient had the plague already in him before inoculation.

tionately to their number, 29 deaths from plague. The actual number appeared reduced by 26, which is *a reduction of* 89·6 *of mortality attributable to inoculation. The result as here obtained tallies with all the observations made up to now upon the protective effect of the plague prophylactic, the reduction of mortality effected by it in a plague-stricken population averaging, with a remarkable regularity*, BETWEEN 80 AND 90 PER CENT."

Then, to finish, take the famous Hubli report, October 1, 1898, by Surgeon-Captain Leumann. It was forwarded to the Plague Commissioners by Mr. E. K. Cappel, Collector of Dhárwár, with this comment:—

"The town of Hubli—a mercantile town of over 50,000 inhabitants—was attacked by plague in an epidemic form at the commencement of the monsoon rains. The average rainfall between April and October amounts to more than 28 inches. Under these circumstances, although a large and weather-proof health camp had been prepared for emergencies, complete evacuation of the infected town-site was impossible; and the attempt to effect it would have led to the severest hardships and to the immediate spread of the disease into surrounding villages and districts. It was for this reason that the determination was formed to make a bold and comprehensive experiment with the prophylactic, and not on any *a priori* grounds. If this experiment had failed, the results, judged by the actual mortality among the uninoculated, would have been appalling. *All possible sanitary measures in the shape of disinfection, unroofing of houses, and segregation, were applied concurrently with inoculation, as Government are already aware; bu the rate of mortality among those who* *held back from inoculation rose at one time to a height which, I believe, has never been approached elsewhere, standing in the third week of September at the figure of* 657 *per thousand per week.*

"However, the experiment, in the hands of Dr. Leumann, did not fail, and it has afforded a demonstration of success which is of Imperial importance. Many thousands of lives have undoubtedly been saved, and at the present moment the plague mortality is merely sporadic, and Hubli is steadily regaining its normal population and trade, though surrounded by infected villages."

The Hubli report must be put at full length, for the vivid picture it gives of plague in India. And it is to be noted that Surgeon-Captain Leumann, who saved Hubli, recognises the supreme importance of other methods than inoculation—disinfection, isolation of cases, evacuation of infected districts :—

"While paying the highest tribute to the value of Mr. Haffkine's inoculation method, which I claim, here in Hubli, to have put to perhaps the severest test to which it has yet been subjected, I am of the opinion that individual protection is, on however great a scale conducted, of less importance to that of general protection and hygiene (considering each method separately, that is to say), for it seems to me more radical, if not more rational, to eradicate a disease than to leave it to pursue its course and only protect people against its ravages."

Sanitation, therefore, is Dr. Leumann's faith. Now for his works :—

"I first started inoculation here on May 11th. . . . When I began my inoculations, I operated first of all on some European or native gentlemen in front of a crowd of poor and low-caste people, whom I had gathered together in the worst-affected area, and they were thus soon induced to ask for inoculation themselves. . . . They have presented themselves, by the hundred, at all times of the day before myself and others, for the purpose of being inoculated.[1] . . . I have never experienced the slightest difficulty in inoculating Mussulmanis or any other purdáh women in Hubli. . . . The very men who, in March last, created a disturbance in Hubli, were not only the first and the most willing to undergo inoculation, but also to bring their wives and families to my hospital, or to invite me to their homes to inoculate them.

"Inoculated persons holding certificates of double inoculation have, at my special wish and order, been left in their homes throughout this epidemic ; only their clothes, house, and property being disinfected on the occurrence of a plague case or death in their house. As the vast majority of plague cases have never been notified before death in Hubli (nor, in my experience of nearly two years, elsewhere, if native supervision be largely resorted to), it will readily be understood that the majority of the inoculated have actually been living in the same house, or even room, with a plague case (often of the pneumonic type, whose terrible power of spreading the disease was first shown by Professor Childe, I.M.S., of Bombay) during the whole of the time that case was living, probably attending on the patient, breathing the same stuffy air, and, perhaps, sharing the same blanket ; and I attach at the end of this report a long series of cases where such conditions have occurred, *the non-inoculated dying of plague, and the inoculated escaping, almost to a man.*

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[1] Compare the account of the inoculations at Gaday, in the *Lancet*, February 11, 1898 : "To see the crowd waiting and struggling to pass the barrier is a strange sight : old men and women, young children, and mothers with babes in their arms, form a daily crowd numbered by hundreds, who wait for hours to get their chance of the day's inoculation."

"Various critics on my work, not knowing what the actual facts were and are, have at different times asserted that the inoculated inhabitants of Hubli left the town in larger numbers than the non-inoculated. Exactly the reverse was the case. The British officers on plague duty here, and all the Divisional Superintendents, invariably replied (officially and in writing when so required) that the non-inoculated left Hubli in far greater numbers and proportion than the inoculated ; and my own observations entirely bear out this statement.

"It has been urged that those who received inoculation were of a class or classes better protected than others against plague by reason of their habits, the food they eat, the houses they live in, &c. In reply, I unhesitatingly state that if there be but one town in India, where that line of argument will not hold good, it certainly is Hubli ; for *not only were the poorer, dirtier, lower-caste people the first to be persuaded to receive inoculation, but I made it my personal and special duty to work amongst them.* My first few thousand inoculations were almost entirely amongst the lowest and poorest of the people. The Brahmins are, perhaps, of all castes, supposed to be the most cleanly in their houses, habits, &c., yet the Brahmins of Hubli (who at first, imagining themselves immune, were the foremost and greatest perverters of the truth concerning its efficacy, and the last to apply for the protection inoculation affords) simply inundated the various inoculation centres, as soon as plague began to spread in their midst, clamouring for the very method of which they had only lately tried to prevent others from availing themselves.

"Unfortunately, the average native, educated or not, appears to have the very greatest aversion to notifying any case of sickness—plague or other—and hence, in my opinion, it becomes more necessary than ever to protect the people by inoculation, since they will not help to protect themselves by the foremost and simplest of sanitary and hygienic measures.[1] With so few police (and those none too good) to help one; an inadequate British Staff;

I

Dates.	Census of Hubli.	Non-inoculated.	Inoculated.	Plague-deaths among Non-inoculated.	Plague-deaths among Inoculated.
Five weeks, from May 11 to June 14	Fell from 50,000 to 47,427	44,573	2,854	47	1
Week ending June 21	47,082	41,494	5,588	22	3
„ „ June 28	47,485	39,042	8,443	29	1
„ „ July 5	46,537	36,020	10,517	55	6
„ „ July 12	46,518	33,255	13,263	34	6
„ „ July 19	45,240	29,716	15,524	82	7
„ „ July 26	43,809	24,112	19,697	100	15
„ „ Aug. 2	43,707	21,031	22,676	140	16
„ „ Aug. 9	42,768	15,584	27,184	272	19
„ „ Aug. 16	40,441	10,685	29,756	386	61
„ „ Aug. 23	39,400	6,367	33,033	371	41
„ „ Aug. 30	38,210	4,094	34,116	328	28
„ „ Sept. 6	38,382	2,731	35,469	227	34
„ „ Sept. 13	38,408	1,116	37,292	138	47
„ „ Sept. 20	39,142	937	38,205	106	55
„ „ Sept. 27	39,315	603	38,712	58	20

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[1] Compare the account given by the Rev. H. Haigh (*Methodist Recorder*, December, 1898) of the plague at Bangalore: "The native population do all they can to elude the vigilance of the authorities. In order to escape segregation, the householders in many instances refrain from reporting plague, and not infrequently bury the corpse secretly. Not only is any spare piece of ground used as a burial place, but the body is at times thrown into a well or tank, or dropped over the wall of some European compound. During one week three plague corpses were found, badly decomposed, in reservoirs commonly resorted to for drinking purposes."

with so much reliance placed in Native Superintendents and Supervisors, and a Municipality so bankrupt that it could not apparently afford to buy enough blankets out of its own funds for the patients in the Plague Hospitals—the work of segregation, house-to-house inspection, &c., became, from a medical point of view, absurdly insufficient.

"The total number of inoculations performed in Hubli,

II

Dates.	Plague death-rate. Comparison per 1,000 between		Percentage reduction of Plague death-rate in favour of the Inoculated.
	Non-inoculated.	Inoculated.	
Five weeks, from May 11 to June 14	1·022	·350	Over 65 per cent.
Week ending June 21	·530	·527	About 1 " "
" " June 28	·742	·118	Nearly 85 " "
" " July 5	1·524	·570	About 63 " "
" " July 12	1·022	·452	Nearly 56 " "
" , July 19	2·793	·450	84 " "
" " July 26	4·147	·761	82 " "
" " Aug. 2	6·656	·705	89 " "
" " Aug. 9	17·325	·698	Over 96 " "
" " Aug. 16	33·694	2·083	94 " "
" " Aug. 23	57·011	1·241	98 " "
" " Aug. 30	80·116	·820	98 " "
" " Sept. 6	83·112	·958	99 " "
" " Sept. 13	112·903	1·260	Over 99 " "
" " Sept. 20	113·127	1·439	Over 99 " "
" " Sept. 27	96·185	·517	Over 99 " "

"It appears that if the 47,427 inhabitants had remained, as they did—in their town, without running away by rail or otherwise, or without camping out in a mass—and if no inoculation had been resorted to—they would have lost 24,899 souls, or a little over a half of their number. The official records show that this has actually occurred, during the present terrible outbreak, in a number of large villages, of 2,000 inhabitants and over, in the Hubli taluka and elsewhere in the Dhárwár District, where no inoculation was done, and no camping-out was possible on account of the wet weather." (Haffkine's commentary on Dr. Leumann's report).

> both on actual inhabitants and on people from outside (villages) between May 11th and September 27th, amounts to some 78,000 altogether."

And these amazing results are taken, by the men who achieved them, as part of the day's work. The plague-bacillus was discovered by Kitasato and Yersin in 1894: they both found it about the same time, but were not working together. Yersin's discovery was made at Hong Kong, where the French Government had sent him to study the plague; the date of his arrival at Hong Kong is June 15th. An excellent account of his work is in the *Annales de l'Institut Pasteur*, September, 1894.

The whole story of the vaccine-treatment against plague cannot be put here—the Austrian, Italian, and English Commissioners, the work of Lustig, Galeotti, and many more. But there are two or three points that must be noted.

1. The *Pioneer Press*, Allahabad, published this year a most admirable pamphlet by Mr. Hankin on the plague, an account of Haffkine's method, written for native readers. He points out how the inoculations are in no way contrary to the laws of caste:—

> "If a minute trace of bouillon, rendered turbid by the growth in it of the bacilli, be transferred to another flask, a precisely similar growth is obtained. The plague microbe may be passed through an indefinite number of flasks of bouillon, and thus may be obtained in pure culture completely free of any substance derived from the patient."

The inoculations contain nothing human, nor do they contain living organisms: their action is chemical. Therefore they do not offend any law of caste.[1]

2. The first inoculations were made on January 30, 1897, in the Byculla House of Correction, Bombay. The method had already been tested on animals, then on a large number of medical men:—

> "Twenty healthy rabbits were put in cages. Ten of them were inoculated with Haffkine's plague vaccine. Then both the vaccinated rabbits and the other ten rabbits that had not been vaccinated were infected with plague. The unprotected rabbits all died of the disease, and in their bodies innumerable quantities of the microbes were found. But the vaccinated rabbits remained in good health. Professor Haffkine then vaccinated himself and his friends. This produced some fever, from which, after a day or two, they recovered. Plague broke out in Byculla Jail, in Bombay, in January, 1897. About half the prisoners volunteered to be inoculated. Of these, three developed plague on the day of inoculation, and it is probable that they had already plague before the treatment was carried out.[2] Of the remaining 148 who were inoculated, only two were afterwards attacked with plague, and both of them recovered. At the same time, of the

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[1] It is said that the Jains object to inoculations on the grounds of religion; and one or two witnesses before the Plague Commission gave evidence to the same effect. But, at Bombay, the high-priest of a great religious community lately addressed a meeting of 5,000 in favour of the new treatment; and the rush of suppliants for inoculation at Hubli and Gaday proves that there is no real religious difficulty. Doctors have been assaulted, as at Poona, so just lately at Oporto; in neither case can we say *Tantum relligio potuit suadere malorum.*

[2] For these three cases, and the evidence that they were already infected at the time of inoculation, see Haffkine's commentary on the Hubli report.

173 who had not been vaccinated, twelve were attacked, and out of these six died."

3. Yersin's name is associated not so much with the preventive method as with the treatment of patients already plague-stricken. He is still at work to improve his serum—*nos méthodes se perfectionnent de jour en jours*—but already it is said to have given good results in China.[1] Unhappily, every hour makes a difference in plague, and what might cure a patient in the first day of the disease might be useless on the second day :—

"Dr. Yersin's report on his late visit to Bombay is published in the *Archives de Médecine Navale et Coloniale* for November, 1897. . . . He treated 17 *cases on the*

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[1] The recent report, by Dr. E. L. Marsh, of the plague at Poona (see *Brit. Med. Journ.*, 1899) gives notes of 4,179 cases admitted to the Poona Plague Hospital between June 1, 1897, and March 31, 1898. Of these 2,836 died (489 of them a few hours after admission), 1,310 recovered, and 33 were left in hospital at the time of the report. In a few cases, and in a few only, Lustig's serum or Yersin's serum was used ; with one serum, the results were "disappointing" ; with the other, "the numbers treated were too few to allow of any criticism of this method of treatment." Truly, with the plague, prevention is better than cure ; for the present it is enough that the preventive treatment saves from the plague, '*with a remarkable regularity*,' between 80 and 90 per cent. The curative treatment has to fight against colossal difficulties, which are at present wholly insuperable. How can it have a fair chance among a native population who will not notify cases, who bring them to hospital just dying ? It has been found that 33 per cent. of admissions to the large plague hospitals die within 24 hours ; they are brought there to die. Shall the curative serum be given to these dying patients or not ? If it is given where it is useless, the treatment is wrong ; if it is given only where it might be useful, then the cases are selected, and the results therefore worthless. According to Haffkine, the curative treatment has at present failed in India, but not in China. Some good results in China are mentioned in the *Brit. Med. Journ.*, January 21, 1899. It is reported that it has given good results during the present epidemic at Oporto (September, 1899).

> *first day of the disease, with a mortality of* 12 *per cent.*; 17 on the second day, with a mortality of 35 per cent.; 12 on the third day, with mortality 50 per cent.; 4 of longer standing, with mortality 75 per cent.; the average death-rate on 50 cases treated being 34 per cent., *a very great improvement on the general ratio, which, among natives, amounted to* 85 *per cent. . . . At Amoy, Dr. Yersin's death-rate was only* 7·6 *per cent.*, or not much more than half his best results in Bombay, and nearly one-fifth of his average mortality in the latter city." (*Lancet*, December 11, 1897).

Doubtless the Amoy plague was a milder form; and these results, anyhow, are nearly three years old. The Nhatrang results have just been published in the *Annales de l'Institut Pasteur*, March, 1899. Nhatrang is an Annamese fishing-village; and the plague, when it was left to itself, killed every case that it got:—

> "La peste s'est montrée excessivement meurtrière chez les Annamites.
>
> "Sur 72 cas de peste, 39 personnes chez lesquelles la maladie a évolué normalement ou qui n'ont été traités que par des médecins indigènes sont mortes sans exception.
>
> "Les 33 autres cas ont pu être traités par le sérum, quelquefois dans de bonnes conditions, mais le plus souvent quelques heures seulement avant la mort. Malgré cela, nous avons obtenu 19 guérisons et 14 décès, ce qui fait une mortalité de 42 per cent. chez les traités.
>
> "*Ainsi, d'une part,* 100 *pour* 100 *de mortalité chez les non traités; de l'autre,* 42 *per cent., chez les malades qui ont reçu au sérum.* Ces chiffres confirment les résultats que j'avais obtenu en Chine en 1896. Si la proportion des morts est encore considérable chez les Annamites, cela tient à leur

peu de résistance, que je n'ai jamais vue si faible ni en Chine ni aux Indes.

"Nous avons largement pratiqué les inoculations préventives avec le sérum, et nous avons pu constater qu'aucune de ces personnes n'a été atteinte.

"L'indigène n'a d'ailleurs jamais compris la gravité de cette maladie, qu'il ignorait jusqu'à ce jour, et dont le nom n'existait même pas. Malgré toutes les instructions, les explications et les exemples des cas traités sous leurs yeux, les annamites attribuent encore aujourd'hui les décès causés par la peste à l'influence surnaturelle des Génies irrités : la pagode de Nhatrang étant habitée provisoirement par le sous-préfet indigène, les habitants sont venus déclarer à l'autorité française que le Génie du village, mécontent de cette usurpation, avait déchainé cette nouvelle maladie. Il a fallu s'incliner devant cette croyance et pourvoir le sous-préfet d'un nouveau local. L'épidémie n'en a pas moins continué. D'autres décès ont eu pour cause la colère de la déesse Baghavati, dont l'esprit serait caché dans un antique monument chame, que tout annamite révère et craint. C'est d'ailleurs par des sortilèges et des incantations que les médecins annamites prétendent combattre la peste, lorsque leurs médecines sont restées impuissantes.

"Il nous est toutefois permis d'espérer que la science n'a pas dit son dernier mot. Nos méthodes se perfectionnent de jour en jour, et il n'est pas impossible que nous arrivons à être maître de la peste comme Jenner l'a été de la variole."

4. At the present time (August, 1899) the plague at Poona is at its worst—*in præcipiti stetit*—and Bombay is again threatened. "The extent and virulence of the outbreak at Poona appear un-

paralleled; the worst week in Bombay chronicled a death-rate of 125 per 1,000 per annum, *but at Poona it has been over 340 per 1,000 per annum.*" (*Lancet*, August 26, 1899.) Of course the preventive treatment, among three hundred millions of people, only touches points here and there on the vast map of India. The protection that it gives may not last very long—perhaps about a year, perhaps more; it is too soon to be sure. In Bombay this year, "notwithstanding the great increase of deaths from plague in Bombay city, inoculation is proceeding very slowly. Only 388 inoculations appear to have been done for the week ending January 20th, and these chiefly among the low-caste Hindus. Last year, when the authorities could have offered inoculation in place of segregation and isolation, they had a powerful lever of encouraging this form of protection. Now that detention and passes have been abolished, and the plague regulations do not frighten the people, there is no leverage of assistance." (*Lancet*, February 15, 1899.)

5. Haffkine's work goes with, not against, the older world-wide ways of fighting the plague—quarantine, notification, isolation, all sanitary measures, destruction of things infected, destruction of rats, evacuation of infected places. Take the opinion of Surgeon-General Harvey, Director-General of the Indian Medical Service, at the discussion on Haffkine's discourse before the Royal Society a few months ago (*Lancet*, July 1, 1899):—

"The people of England should consider the difficulties attending the work of a bacteriologist in India. . . . He had no doubt as to the value of the inoculations. At Undhera he carefully examined the results of the experiment, and, as far as he could judge, there was no possibility of error. The results in that experiment were such as to be 90 per cent. in favour of the inoculated against the uninoculated. The natives of India were, however, a strange people, and it was difficult to prophesy how they would act. In Calcutta, the mention of inoculations had driven in hot haste from the city 300,000 people, many of whom afterwards returned and were inoculated; while at Hubli he had seen the inhabitants come in their thousands to be inoculated and pay for the inoculations. The medical officer in charge at Hubli had performed about 80,000 inoculations, and had only observed some 12 abscesses. He thought that 12 abscesses only, in 80,000 inoculations, showed good results. But, after all, what were the numbers of inoculations performed to the 300,000,000 inhabitants of India? He felt that even if every one consented to be inoculated it was impossible to provide the vaccine or the medical officers for such a demand. It was accordingly to sanitary improvements that he looked with the most confidence to protect India against the plague."

But for sudden outbursts of plague—since rats seem to be the principal source of infection—*le rat, le génie de la peste*—since notification is fundamentally abhorrent to native habit—since evacuation may ruin trade, or spread infection, or be impossible by reason of the rains—since "East is East, and West is West"—it is not always possible to provide, for an Indian village smitten by plague, the excellent arrangements that Gloucester is making for the next outbreak of small-pox.

6. In a few instances it has been found that samples of the serum have become unwholesome by contamination with other chance organisms. But at Hubli no less than 80,000 inoculations were made, with only 12 cases where the inoculation was followed by abscess. The technical difficulties, in India, in the way of supplying the demand for the serum, are of course very great, and at times insuperable.

7. The real opposition to inoculations, in India, does not come from caste, but from a few people who repeat and believe the nonsense printed by the *Zoophilist* and the *Abolitionist* in England; and from other prejudiced critics. For instance, on April 11, 1898, a meeting of native hakims at Masti, Lahore, passed the following resolutions :—

> "That in the opinion of this meeting the bubonic plague is not a contagious disease. It originates from poisoned air, and this poison is created in the air on account of atmospherical germs and the excess of terrestrial humidities.
>
> "That this meeting, having carefully considered the Resolution of the Punjab Government (January 11, 1898), is of opinion that the rules embodied in that Resolution (isolation, disinfection, &c.) are unnecessary under the principles of Unani medical science."

And among statements to be made to the Plague

Commissioners was the following, from a native practitioner in Bombay (April, 1899):—

> "I do not think the plague was imported in Bombay from Hong Kong or anywhere else. I attribute three sources of causes of outbreaks of plague in Bombay; (*a*) The predisposing cause was the Bombay Municipality. (*b*) The exciting cause was the Nature herself. (*c*) The aggravating cause was the Plague Committee."

All these facts,[1] from official reports and medical journals, give no idea of the courage and self-sacrifice of the men and women who are fighting the plague in India. The story of their work should be read in that most excellent paper, the *Indian Medical Gazette*. Here we are concerned only to note that the whole thing has come out of experiments on animals: that the mortality in a plague-stricken place may be reduced, "with a remarkable regularity," between 80 and 90 per cent. in favour of the inoculated; and that the Secretary of State for India has lately asked Parliament to consider this fact, that the saving of life in India has become something really alarming.

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[1] For more recent statements, see Appendix. Also the report on the Belgaum inoculations, by Lt.-Col. Bennett and Major Bannerman, I.M.S., published in the *Indian Medical Gazette*, June, 1899.

X

TYPHOID FEVER

THE names of Klebs, Eberth, and Koch are associated with the discovery, in 1880–81, of the typhoid-bacillus. Since that time it has been studied from every point of view; in animals—in the blood, tissues, and excretions—in earth, air, water, milk, food, and sewage. The bacteriology of typhoid fever has a whole literature to itself: and experimental work has already borne fruit here both for science and for practice.

The date of the first protective inoculations against typhoid is July–August, 1896: they were made at Netley Hospital, by Professor Wright and Surgeon-Major Semple. The first inoculations in Germany, made by Pfeiffer and Kolle, were published two months later. The story of these famous Netley inoculations is told in the *British Medical Journal*, January 30, 1897. Eighteen men offered themselves—

> "A good deal of fever was developed in all cases, and sleep was a good deal disturbed. These constitutional symptoms had to a great extent passed away by the morning, and laboratory work went on without interruption. . . . With two exceptions, all these vaccinations were performed upon Medical Officers of the Army or Indian Medical Services, or upon Surgeons on Probation who were preparing to enter those services."

Good luck attend all eighteen of them, and immunity against typhoid, wherever they are. The doses that they received were estimated in proportion to the dose that would kill a guinea-pig of 350–400 grammes weight; and the protective fluid contained no living bacilli :—

> "The advantages which are associated with the use of such 'dead vaccines' are, first, that there is absolutely no risk of producing actual typhoid fever by our inoculations; secondly, that the vaccines may be handled and distributed through the post without incurring any risk of disseminating the germs of the disease; thirdly, that dead vaccines are probably less subject to undergo alterations in their strength than living vaccines."

Later, by another method of preparing the vaccine, the ill effects of inoculation were reduced to a minimum : "and now all that is felt is a few hours' discomfort and a little local soreness."

The first use of the vaccine during an outbreak of typhoid was in October, 1897, at the Kent County

Lunatic Asylum. The treatment was offered to any of the working staff who desired it :—

> "All the medical staff, and a number of attendants, accepted the offer. *Not one of those vaccinated*—84 *in number—contracted typhoid fever: while of those unvaccinated and living under similar conditions,* 16 *were attacked.* This is a significant fact, though it should in fairness be stated that the water was boiled after a certain date, and other precautions were taken, so that the vaccination cannot be said to be altogether responsible for the immunity. Still, the figures are striking." (*Lancet*, March 19, 1898; see also Dr. Tew's paper, in *Public Health*, April, 1898.)

Certainly, they are striking ; so is the story of the eight young subalterns on the Khartoum expedition, of whom six were vaccinated, and two took their chance. The six escaped typhoid, the two were attacked by it, and one died. This year (1899) Professor Wright is in India, on the Plague Commission, and has vaccinated against typhoid more than three thousand of our troops, at Bangalore, Rawal Pindi, and Lucknow.[1] Typhoid among our young soldiers in India is on the increase: in 1897, among all causes of death to British troops in India, typhoid alone claimed 37 per cent. It is the young Englishmen who are killed ; the native population enjoys a considerable degree of natural immunity. On August 1st of the present year, questions were asked in the House of Commons about this very serious risk of our soldiers; and the Secretary of State for India, in his reply, said—

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[1] For more recent inoculations, see *British Medical Journal*, September 23, 1899.

> "Voluntary inoculation against enteric fever, at the public expense, among the British troops in India, has now been sanctioned."

And, for a good commentary on this decision of Government, we have the admirable address at Netley, July 29th, by Sir George White, V.C., Quartermaster-General to the Forces. (*Lancet*, August 12, 1899).

But this preventive treatment is only a part of what has been done. Wright and Semple and Durham here, Chantemesse and Widal in France, Pfeiffer and Kolle and Grüber in Germany, and a host of other men, working on the same lines, have achieved much more than a method of protection. They have found "Widal's reaction": and the practical uses of this reaction are of very great importance.

Widal's reaction is surely one of the fairy-tales of science. The bacteriologist works not with anything so gross as a drop of blood, but with a drop of blood fifty or more times diluted; one drop of this dilution is enough for his purpose. Take, for instance, an obscure case suspected to be typhoid fever: a drop of blood taken from the finger is diluted fifty or more times, that the perfect delicacy of the test may be ensured; a drop of this dilution is mixed with a drop of nutrient fluid containing living typhoid bacilli, and a drop of this mixture of blood and bacilli is watched under the microscope :—

> "The motility of the bacilli is instantaneously or very quickly arrested, and in a few minutes the bacilli begin to aggregate together into clumps, and by the end of the half-hour there will be very few isolated bacilli visible. In less marked cases, the motility of the bacilli does not cease for some minutes ; while in the least marked ones the motility of the bacilli may never be completely arrested, but they are always more or less sluggish, while clumping ought to be quite distinct by the end of the half-hour."

The result of this clumping is also plainly visible to the naked eye, by the subsidence of the agglutinated bacteria to the bottom of the containing vessel : and thus an easy practical mode of diagnosis is afforded by it.

As with typhoid, so with Malta fever, cholera, and some other infective diseases. And the unimaginable fineness of this reaction goes far beyond the time of the disease. Months, even years, after recovery from typhoid, a fiftieth part of a drop of the blood will still give Widal's reaction : and it has been obtained in an infant whose mother had typhoid before it was born. A drop of dried blood, from a case suspected to be typhoid, may be sent a hundred miles by post to be tested ; and typhoid, like diphtheria, may now be submitted to the judgment of an expert far away, and the answer telegraphed back.

The first systematic study of this subject was made by Durham and Pfeiffer; and Widal's name is especially associated with the application of their work to the uses of practice. The whole history of the discovery is given by Dr. Cabot in his book *The Serum-Diagnosis of Disease* (London and Bombay: Longmans, Green & Co., 1899).

Thus, within a few years, experiments on animals have set the whole subject of typhoid in a new light. They have given to everybody a new method for the early diagnosis of obscure cases. They have illuminated some of the mysteries of immunity; and they have brought about preventive inoculation.

NOTE.

1. For a good instance of the practical value of "Widal's reaction," see Dr. Naegeli's account ot an outbreak of typhoid in an asylum in Switzerland. (*Lancet*, Sept. 23, 1899.)

2. "The loss of 616 young soldiers' lives in one year is a very serious matter. Besides the waste of life, the total loss of service is enormous. Compared with enteric fever, the danger of smallpox is infinitesimal." (*Lancet*, Special Correspondent in India, July 15, 1899.)

3. Mr. Foulerton has lately published an excellent account of the whole subject, in the *Middlesex Hospital Journal*, October, 1899.

4. For an estimate of the terrible frequency of typhoid among young Englishmen in India, see the

admirable paper by Surgeon-General Harvey, Director-General of the Indian Medical Service, published in the *Indian Medical Gazette* for July of this present year.

Facilities have now been provided in London for the inoculation against typhoid of those who desire to be thus safeguarded in remote parts of the Empire. It is too soon, at present, to know how long the protection lasts. And it may well be, that the clear and final proof of the value of this method will come when some English town suffers as Maidstone and Worthing lately suffered. Then we shall see the parallel case to what happened at Gloucester when small-pox broke out there.

XI

MALTA FEVER. YELLOW FEVER. MALARIA

MALTA FEVER.

THE specific organism of Malta fever (Mediterranean fever), the *bacillus Melitensis*, was discovered in 1887 by Surgeon-Major David Bruce, of the Army Medical Staff. Its nature and action were proved by the inoculation of monkeys. The use or Widal's reaction is of great value in this disease :—

> "The diagnosis of Malta fever from typhoid is, ot course, a highly important practical matter. It is exceedingly difficult in the early stages." (Manson, *loc. cit.*)

As with typhoid, so with Malta fever, Netley led the way to the discovery of an immunising serum. In the course of the work, one of the discoverers was by accident infected with the disease :—

> "He was indisposed when he went to Maidstone to undertake antityphoid vaccination, and after fighting

against his illness for some days, he was obliged to return to Netley, on October 9th. Examination of blood-serum (Widal's reaction) showed that he was suffering from Malta fever. It appears that he had scratched his hand with a hypodermic needle on September 17th, when immunising a horse for the preparation of serum-protective against Malta fever; and his blood, when examined, had a typical reaction on the micrococcus of Malta fever in 1,000-fold dilution. The horse, which has been immunised for Malta fever for the last eight months, was immediately bled, and we are informed that the patient has now had two injections, each of 30 cub. cm. of the serum. He is doing well, and it is hoped that the attack has been cut short." (*British Medical Journal*, October 16, 1897.)

A good instance of the value of the serum-treatment ot Malta fever is published in the *Lancet*, April 15, 1899. About fifty cases have now been treated at Netley "with marked benefit: whereas they round that all drug-treatment failed, the antitoxin treatment had been generally successful."[1]

YELLOW FEVER.

In the army of men who have experimented on themselves, those who first studied yellow fever are to be counted:—

"In 1816, Dr. Chervin, of Point-à-Pitre (Antilles), drank repeatedly large quantities of black vomit without feeling the least disturbance. Some years before, other

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[1] For the whole subject, see *Lancet*, Sept. 9, 1899, paper by Surgeon-Major Birt and Surgeon-Captain Lamb. Two other cases of accidental inoculation occurred at Netley.

North American colleagues, Doctors Potter, Firth, Catterall, and Parker, did everything possible to inoculate themselves with yellow fever. After having uselessly attempted experiments on animals, they experimented on themselves, inoculating the black matter at the very moment in which the moribund patient rejected it, placing this matter in their eyes, or in wounds made in their arms, injecting it more than twenty times in various parts of their body ; . . . in short, devising every sort or daring means for experimentally transmitting yellow fever. All these experiments were without result, and in the United States during many years it was believed that this terrible malady was non-contagious." (Sanarelli, quoted in *British Medical Journal*, July 3, 1897.)

Finlay, Sternberg, Havelberg, and others, have worked at yellow fever, but Sanarelli's name is alone associated with the discovery of a specific organism, the *bacillus icteroides*, and with the work of preparing an immunising serum. He began his study of yellow fever in February, 1896, in the lazaretto on the island of Flores. He did not spare himself in the course ot his experiments, and he nearly died over the work. At Flores he discovered the bacillus ; in June he went to Rio Janeiro, and studied the disease there. By a long series of experiments on animals, he established the exact pathology and course of it ; and in 1897 he showed that "Widal's reaction" could be employed as a test in cases of the disease. By October of that year (*Annales de l'Institut Pasteur*, October, 1897) he had prepared an immunising serum, which was able to give a considerable amount of protection to animals :—

> "This serum was tried, directly after it had been obtained, on guinea-pigs, against a mortal dose of virulent cultures. Half a cubic centimetre of this serum, injected 24 hours before the dose of virulent cultures, gave immunity. Two centimetres of it succeeded in saving guinea-pigs already ill, even if it were injected 48 hours afterward. These doses are still far from representing the full preventive and curative power of the serum, especially if one takes count of the power of the other sera prepared up to the present time. . . .
>
> "Such are the results hitherto obtained by laboratory work on the specific treatment of yellow fever. The preventive and curative power of the serum of the guinea-pig, the dog, and the horse, vaccinated against the bacillus icteroides, should be held as absolutely demonstrated in the case of animals."

Next year (*Annales de l'Institut Pasteur*, May, 1898) came the news that he had advanced against yellow fever with its own weapons—*Premières expériences sur l'emploi du sérum curatif et préventif de la fièvre jaune.* Of the first eight cases treated (Rio de Janeiro) four recovered. Then came the 22 cases at San Carlos do Pinhal, in Saint-Paul au Brésil (January, 1898), with 16 recoveries, and only 6 deaths. And it is to be noted that he submitted his method of treatment to the utmost test that was possible ; he chose the bad cases, and the country where the fever was most fatal :—

> "Chaque cas était choisi de commun accord entre nous,

dans le but de mettre bien en évidence l'action thérapeutique du sérum, *mettant toujours de côté tous les cas qui se présentaient avec des symptômes vagues ou atténuès ou en forme légère ou fruste. On ne conservait donc que des cas oû, d'après la violence des phénomènes d'invasion, on devait considérer comme très peu probable une crise spontanée de la maladie.* . . .

"L'Etat de Saint-Paul, le plus riche de la République brésilienne, pays d'immigration, traverse aujourd'hui une triste période, depuis que la fièvre jaune, qui jusqu'à ces dernières années n'avait pas quitté les côtes, s'est diffusée et a envahi comme un incendie presque toutes les villes et presques tous les villages de l'intérieur, semant des ruines partout.

"La fièvre jaune est bien plus grave à l'intérieur du pays, et atteint une mortalité bien plus élevée que celle qu'on observe dans les côtes, par exemple, à Rio de Janeiro, à Santos, ou à Pernambuco. Dans ces dernières villes, les immigrants en général ne séjournent pas ; la fièvre jaune atteint en général des indigènes, ou tout au moins des gens relativement *acclimatés* par un séjour plus ou moins long, et la mortalité ne dépasse pas 50 à 60 % des malades. Dans l'intérieur du pays, au contraire, la maladie trouve un élément neuf, européen, récemment arrivé, non encore habitué au climat et au genre de vie des pays intertropicaux, et par suite extrêmement faible et sans défense. *La mortalité est d'alors* 80 *ou* 90 % *des malades*, et il y a eu à Campinas, à Rio-Claro, à Araraquara, et sur d'autres points, des épidémies comparables seulement aux invasions légendaires de la peste au moyen âge."

The serum used by Sanarelli at San Carlos came from three animals, two horses and an ox, that he had long kept immunised. He had tested it on animals,

and on himself. At the isolation hospital he found only two children :—

> "La plupart des gens préféraient rester chez eux pour mourir ; les seuls malades à ce moment à l'hôpital étaient deux enfants nommés Louis et Assunta del V. . . . ramassés dans la maison où leur père était déjà mort de fièvre jaune. Ces deux petits malades présentaient les symptômes caractéristiques de la maladie, y compris le *vomito negro ;* Louis était au second jour et Assunta au troisième de la maladie. Ils furent soumis de suite au traitement, dont les résultats furent presque immédiats ; la fièvre et l'albuminurie disparurent, les symptômes généraux s'atténuèrent et les deux enfants entrèrent en franche convalescence."

Sixteen recoveries, out of twenty-two cases, in a country where the mortality under any other treatment is reckoned at 80 or 90 per cent. And, of the six who died, four were indeed hopeless from the first.

Furthermore, Sanarelli was able to show the preventive value of the serum. At the end of February, 1898, yellow fever broke out in the jail at San Carlos :—

> "La première victime fut un condamné, qui vivait avec tous les autres dans une salle où les conditions hygiéniques étaient assez mauvaises. Le lendemain, la sentinelle, qui était en rapport continuel avec la salle des condamnés, tombait malade. Quelques jours après, un autre condamné suivait le sort du premier, et bientôt un quatrième cas, mortel aussi, finit par signaler la prison comme un nouveau foyer d'infection qui venait s'allumer au centre d'un quartier de la ville encore resté indemne.

"Si on avait abandonné la chose à elle-même, on aurait vu se produire le même spectacle qu'avaient fourni, dans les conditions identiques, pendant les dernières épidémies, les prisons de Rio-Claro, de Limeira, et d'autres villes de l'État de Saint-Paul."

Every prisoner, except one who had already had the fever, was therefore given the preventive treatment. At once the outbreak stopped; no more cases occurred, though only a weak serum was used, though the state of the prison and its occupants was unhealthy, though the fever, two months later, was still raging, round the prison, in the town.[1]

MALARIA.

The *plasmodium malariæ*, an amœboid organism, was discovered by Laveran in 1880, in the blood of malarial patients. For many years his work stopped there, because it was impossible to find the *plasmodium* in animals: "the difficulties surrounding the subject were so great that this discovery seemed to be almost hopeless." In 1894, Dr. Patrick Manson—who had proved mosquitoes to be the intermediate host in the case of the parasitic nematode *filaria*—suggested, as a working theory of malaria, that the plasmodium was carried by mosquitoes. This belief, not itself new, he made current coin. He observed that there is a flagellate form of the plasmodium, which only comes into existence after the blood has left the body:

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[1] For the recent report, from Havana, of the United States Yellow Fever Commission, see *Lancet*, Sept. 30, 1899.

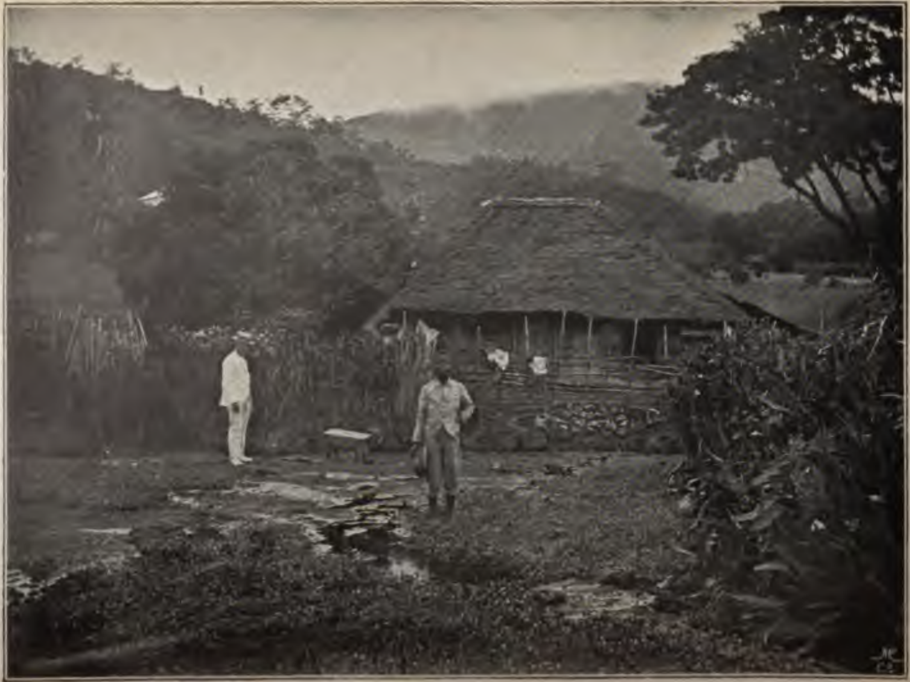
and he suggested that the flagella might develop in the mosquito as an intermediate host, a halfway-house between man and man. Then, in 1895, Surgeon-Major Ronald Ross, I.M.S., set to work in India, keeping and feeding vast numbers of mosquitoes on malarial blood; and for two years without any conclusive result. About this time came MacCullum's observations, at the Johns Hopkins University, on a parasitic organism, *halteridium*, closely allied to the plasmodium malariæ; he showed that the flagella of the halteridium are organs of impregnation, having observed that the non-flagellated form, which he regarded as the female, after receiving one of the flagella, changed shape, and became motile. In August, 1897, Surgeon-Major Ross found bodies, containing pigment like that of the malarial parasite, in the outer coat of the stomach of one kind of mosquito, the grey or dapple-winged mosquito, that had been fed on malarial blood. In February, 1898, he was put on special duty under the Sanitary Commissioner with the Government of India, to study malaria, and started work again in Calcutta :—

> "Arriving there at a non-fever season, he took up the study of what may be called 'bird malaria.' In birds, two parasites have become well known—(1) the halteridium, (2) the proteosoma of Labbé. Both have flagellated forms, and both are closely allied to the plasmodium malariæ. Using grey mosquitoes and proteosoma-infected birds, Ross showed by a large number of observations that it was only from blood containing the proteosoma that

pigmented cells in the grey mosquito could be got; therefore that this cell is derived from the proteosoma, and is an evolutionary stage of that parasite. Next, Ross proceeded to find out its exact location, and found that it lay among the muscular fibres of the wall of the mosquito's stomach. It grows large (40–70 micromillimetres) and protrudes from the external surface of the stomach, which under the microscope appears as if covered with minute warts." (Manson, at Edinburgh meeting of British Medical Association, 1898.)

These pigmented spherical cells give issue to innumerable swarms of spindle-shaped bodies, "germinal rods"; and in infected mosquitoes Ross has found these rods, in the glands that communicate with the proboscis. Thus the evidence appeared complete, that the plasmodium malariæ, like many other parasites, had a special intermediate host for its intermediate stage of development; and that this host was the dapple-winged mosquito. It is impossible to over-estimate the infinite delicacy and difficulty of Ross's work; for instance, in his "Abstract of Recent Experiments with Grey Mosquitoes," he says that "out of 245 grey mosquitoes fed on birds with proteosoma, 178, or 72 per cent., contained pigmented cells; out of 249 fed on blood containing halteridium, immature proteosoma, &c., not one contained a single pigmented cell." Another time (April, 1898) he counted these pigment-cells under the microscope:—

"Ten mosquitoes fed on the sparrow with numerous



Photograph taken at Grassfields, Sierra Leone, by a member of the Malaria Expedition (Liverpool School of Tropical Medicine): showing one of the breeding-puddles of Anopheles.

proteosoma contained 1,009 pigmented cells, or an average of 101 each. Ten mosquitoes fed on the sparrow with moderate proteosoma contained 292 pigmented cells, or an average of 29 each. The mosquitoes fed on the sparrow with no proteosoma contained no pigmented cells."

Finally, he completed the circle of development, by infecting healthy sparrows by causing mosquitoes to bite them.

On July 31st of this present year, Surgeon-Major Ross and the other members of the malaria expedition (Liverpool School of Tropical Diseases) left Liverpool for Sierra Leone. A good account of his work was given in August by Dr. Thin, President of the section of Tropical Diseases, at the Portsmouth meeting of the British Medical Association.

Italy, of course, has given infinite study to malaria; Bignami, Bastianelli, Celli, and Grassi, and many others, have done most valuable work on the mosquitoes of Italy. The chief offender among the Italian mosquitoes is "Anopheles claviger"; the dapple-winged mosquito is different from it, more like "Anopheles pictus," but 2 mm. shorter.

Thus, in a few years, the cause of malaria has been found:—

"If this be so, the prevention of malaria will depend upon the prevention of mosquito-bites. This may not be so difficult as is supposed, because, at any rate as regards several species, mosquitoes have a limited area of propagation, in barrels of water, puddles, and ditches. . . . In the meantime, it may be stated that there is good ground for the belief that the commoner species of mosquito cannot convey the organism of human malaria." (*Indian Medical Gazette*, June, 1899.) See also Appendix.

It is, at least, something gained, that in malaria men have to reckon "not with a nameless something, but with a definite parasite. *Above all things, we must shut off the sources of infection.*" Henceforth the measures against malaria will be directed against mosquitoes and their haunts, puddles and ditches, stagnant pools, with algæ in them, near houses; and the winter habits of *anopheles claviger* have already been studied in Italy as a matter of vital importance to the nation. It is said that, in Italy alone, malaria keeps nearly five million acres of ground from cultivation, affects more or less 63 provinces and 2,823 communes, and every year poisons about two million people, killing fifteen thousand of them.

An informal report from the Sierra Leone expedition has just been published (see daily papers, September 27, 1899). Surgeon-Major Ross writes :—

> "We have now practically finished our work here. We have found—
>
> "(*a*) That local species of Anopheles (mosquitoes) carry malaria.
>
> "(*b*) That these species breed in a few stagnant puddles.
>
> "These observations support my inaugural lecture at every point. Needless to say, we have been most excep-

tionally lucky, to have done so much in so short a time. We shall, of course, wind up with a scientific report to the Committee. The practical results to be derived from the facts which we have obtained will depend solely on the Government and medical profession here. Fortunately Major Nathan is taking great interest in our work, and so are the Colonial doctors. Of course we could kill most of the Anopheles grubs here in a few hours with kerosene oil, and the thing will be done shortly after Ould arrives. But this won't be enough. It is necessary that the operations be continued systematically, and that some of the more dangerous puddles be drained, costing a trifle. Consequently the Governor asked us to advise. I suggested that one of his medical officers be put in charge of operations against the mosquito, and that he be given a trustworthy native assistant. The proposal is before the Governor.

"For many scientific reasons, we have come to the conclusion that the truly malarial fever is caused here solely by the mosquito—probably entirely by the Anopheles species. We estimate, then, that most of the malarial fever here can be got rid of at almost no cost, except of a little energy on the part of the local authorities.."

Before leaving the subject of malaria, it must be added that the discovery and study of the parasite which causes it have cleared up the mystery of the specific action of quinine upon the disease. It operates simply by its germicidal effect upon the microbe. But beyond this we have now a clue which we never had before to guide us to the most advantageous manner of administering the drug.

Glanders in horses, rinderpest, and Texas fever in cattle, have all been worked out by the experimental method. The medical journals of the present year contain many reports on rinderpest from diverse parts of the world—Cape Colony, Hong Kong, Bareilly—especially the report by Dr. Edington, Director of the Bacteriological Institute of Cape Colony, "A Retrospect of the Rinderpest Campaign in South Africa." (*Lancet*, February 11, 1899.) In Cape Colony alone, about half a million cattle have been immunised against rinderpest by one method or another, and the lives thus saved must be reckoned by many thousands.

XII

PARASITIC DISEASES

1. Vegetable Parasites.

OF these, the most important is the *streptothrix actinomyces*, the cause of actinomycosis in man and cattle. Israel, in 1877, gave the first accurate account of it in man: and Böllinger, the same year, studied it in cattle. Ponfick, in 1882, recognised the identity of the disease in man and animals. In 1885, Israel published the collected records of thirty-seven cases in man, tabulated according to the site of the primary infection. Boström, about this time, made cultures of the fungus: but all the earlier attempts at inoculation failed; and it was not till 1891 that Wolff and Israel published their successful inoculations, and thus completed the evidence that actinomycosis is a parasitic infection, a growth of vegetable threads and spores, transmissible between men and animals, and able to keep its vitality outside its host: so that men who are employed with cattle, or have the habit of chewing straws or ears of corn, incur some risk of infection. Before 1877, the disease was hardly suspected in man, and was not understood in cattle.

2. Animal Parasites.

Actinomycosis is a rare disease: but disease from animal parasites is terribly common. The blood-parasites, such as filaria and Bilharzia, were discovered and worked out by methods more or less independent of experiments on animals: they do not come to be considered here. But the grosser parasites—tape-worms and the like—were explained and understood by means of experiments on animals: by this method, and by this alone, their life-history was discovered. They were known to Aristotle and to Hippocrates; but nothing was understood about them. They were never studied, for this among other reasons, that men believed in spontaneous generation; and the presence of lower forms of life inside human bodies was attributed to the fault of the patient, the intemperature of the air, or the work of the devil. Then, at last, Redi (1712), and Swammerdam (1752) in his *Bibel der Natur*, struck at the doctrine of spontaneous generation, saying that it did not apply to insects; and in 1781 Pallas boldly declared that the internal parasites of man came out of eggs, like insects, and not "of themselves." It would be a good theme for an essay—*The paralysing effect, on medicine and* *surgery, of the doctrine of spontaneous generation*; and, so late as 1876, it was upheld in this country against the findings of bacteriology.

Rudolphi (1808) and Bremser (1819) opposed Pallas; and von Siebold (1835) and Eschricht (1837) supported him. Then came the great students of this part of biology — Cobbold, Busk, Davaine, van Beneden, Leuckart, Küchenmeister. In 1842, Steenstrup had discovered, in certain insects, the alternation of generations: in 1852, Küchenmeister proved that the generations of internal parasites are similarly alternate. By feeding carnivorous animals with "measly" meat, he produced tapeworms in them; and by feeding herbivorous animals with the ova of tapeworms, he made their muscles "measly."

The feeding of animals was the only possible way to understand the bewildering transformations and transmigrations of the thirty or more entozoa to which flesh is heir. This chapter of pathology makes up in tragedy what it lacks in romance: for these animal parasites have killed whole hosts of people. Take, for instance, the *trichina spiralis*, a minute worm discovered in 1833 encysted in countless numbers in the muscles of the human body; it was studied by Leuckart and others, by feeding-experiments on animals, and was proved to come from infected half-cooked ham and pork, and to make its way from the alimentary canal all over the body. The name ot trichiniasis or trichina-fever was given to the acute illness that came of the sudden dissemination of these myriad parasites into the tissues. Trichiniasis had killed hundreds of people by a most painful death; outbreaks of it, in Germany and elsewhere, had swept through villages like cholera or plague: then Leuckart traced it to its source, and it was stopped there—*Above all things, we must shut off the sources of the infection*—the butchers' shops were kept under sanitary inspection, people were warned against half-cooked ham and pork, and there was an end of it.

Or take hydatid disease, which occurs in all parts of the world, and in some countries (Australia, Iceland) is terribly common. The nature of this disease—that it is an animal parasite transmissible between men and dogs—was proved by feeding-experiments on animals. In Iceland, where men and dogs live crowded together in huts, there is an appalling number of deaths from hydatid disease; Leuckart, in 1863, said of it—

> "At present, almost the sixth part of all the inhabitants annually dying in Iceland fall victims to the echinococcus epidemic."

Before Küchenmeister's experiments in 1852, there was no general knowledge of the exact pathology of entozoic disease. The advance was made not by the experimental method alone; other things helped: but among them were neither clinical experience, nor "the observation of the just facts of anatomy and or natural motions."

XIII

MYXŒDEMA

ON October 4, 1873, Sir William Gull read a short paper before the Clinical Society of London, "On a Cretinoid State supervening in Adult Life in Women." This famous first account of myxœdema was based on five cases: it is less than five pages long, it does not suggest a name for the disease, and it says nothing about the thyroid gland. Four years later (October 23, 1877) Dr. Ord read a paper before the Medico-Chirurgical Society of London, "On Myxœdema; a term proposed to be applied to an essential condition in the 'Cretinoid' Affection occasionally observed in Middle-aged Women." His work had begun so far back as 1861: and in this 1877 paper he gave not only clinical observations, but also pathological and chemical facts; and he noted, as one among many changes, wasting of the thyroid gland. He also pointed out the close resemblance between cases of myxœdema and cases of sporadic cretinism.

In 1882, Reverdin stated before the Medical Society of Geneva that signs like those of myxœdema had been observed in some cases of removal of the thyroid gland on account of disease (goître). In April, 1883, Kocher of Berne read a paper on this subject, before the Congress of German Surgeons; but he attributed this myxœdema after removal of the gland (cachexia strumipriva) not directly to the loss of thyroid-tissue, but rather to some sort of interference with free respiration, due to operation. On November 23, Sir Felix Semon brought the subject again before the Clinical Society; and on December 14, 1883, the Society appointed a Committee of Investigation to study the whole question.

Their Report, 215 pages long, with tabulated records of 119 cases of myxœdema, was published in 1888. It is a monument of good work, historical, clinical, pathological, chemical, and experimental. Twenty years ago, the purpose of the thyroid gland was unknown: a few experiments had been made on it, by Sir Astley Cooper and others, and had failed; and Claude Bernard, in his *Physiologie Opératoire* (published in 1879, soon after his death), makes it clear that nothing was known in his time about it. He is emphasising the fact that anatomy cannot make discoveries in physiology:—

"The descriptive anatomy, and the microscopic characters, of the thyroid gland, the facts about its blood-vessels and its lymphatics—are not all these as well known in the thyroid gland as in other organs? Is not the same thing true of the thymus gland, and the suprarenal capsules? *Yet we know absolutely nothing about the functions of these organs—we have not so much as an idea what use and importance they may possess—because experiments have told us nothing about them*; and anatomy, left to itself, is absolutely silent on the subject."

Therefore, in 1882–83, things stood at this point—that the removal of a diseased thyroïd gland had been followed, in some cases, by a train of symptoms such as Sir William Gull had recorded in 1873. Would the same symptoms follow removal of the healthy gland? The answer was given by Mr. Horsley's experiments, begun in 1884. He was able, by removal of the gland, to produce in monkeys a chronic myxœdema, a cretinoid state, the facsimile of the disease in man: the same symptoms, course, tissue-changes, the same physical and mental hebetude, the same alterations of the excretions, the temperature, and the voice. It was now past doubt that myxœdema was due to want of thyroid-tissue, and to that alone; and that "cachexia strumipriva" was due to the loss, by operation, of such remnants of the gland as had not been rendered useless by disease.

The advance had still to be made from pathology to treatment. Here, so far as this country is concerned, honour is again due to Mr. Horsley. On February 8, 1890, he published the suggestion that thyroid-tissue, from an animal just killed, should be transplanted beneath the skin of a myxœdematous patient :—

> "The justification of this procedure rested on the remarkable experiments of Schiff and von Eisselsberg. I only became aware in April, 1890, that this proposal had been in fact forestalled in 1889 by Dr. Bircher, in Aarau. (The date of Dr. Bircher's operation was January 16, 1889.) Kocher had tried to do the same thing in 1883, but the graft was soon absorbed ; but early in 1889 he tried it again, in five cases, and one greatly improved."

The importance of this treatment, by transplantation of living thyroid-tissue, must be judged by the fact that in 1888 no practical use had yet been made of the scientific work that had been done. The Clinical Society's Report, published that year, gives but half a page to treatment, of the old-fashioned sort ; and not a word of hope.

Then, at last, in 1891, came Dr. George Murray's paper in the *British Medical Journal*, "Note on the Treatment of Myxœdema by Hypodermic Injections of an Extract of the Thyroid Gland of a Sheep." Later, hypodermic injections of thyroid-extract gave way to sandwiches made with thyroid-gland (Dr. Hector Mackenzie, and Dr. Fox of Plymouth), and these in their turn were eclipsed by tabloids.[1]

It is a strange sequence, from 1873 onward : clinical observation, *post-mortem* work, calamities of surgery, experimental physiology, transplantation, hypodermic injections, sandwiches, and tabloids. And far more has been achieved than the cure of myxœdema. Even if the discovery stopped here, it would still be a miracle that little bottles of tabloids should bring men and women back from myxœdema to what they were before they became thick-witted, slow, changed almost past recognition, drifting toward idiocy. But it does not stop here. The same treatment has given good results in countless cases of sporadic cretinism, restoring growth of body and of mind to children that were hopelessly imbecile. It is of great value also for certain diseases of the skin. Moreover, physiology has gained knowledge of the purpose of the thyroid gland; and a clearer insight into the facts relating to internal secretion.

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[1] It remains only to isolate, even more perfectly, the active principle or principles of thyroid-tissue : Blum's "thyreo-iodin" is perhaps a step in this direction.

Myxœdema is but one instance how the treatment of disease must have the help of experiments on animals. Those who oppose all such experiments, now that they have faced or outfaced the facts about myxœdema, must face the facts about cancer. They know that practice has, for the present, said all that it has to say: that neither clinical experience, nor *post-mortem* work, nor organic chemistry, nor physiology, has found any cure other than operation: that experiments on animals have in the last few years given certain results that cannot be denied or explained away: that never since the world began have men got so near as they are now to this discovery that a man would gladly die to make. What do they wish to see done? They are absolutely ignorant of the elementary facts about the disease: will they advise the experts what line to follow?

XIV

THE ACTION OF DRUGS

LONG after the Renaissance, the practice of medicine was still under the influence of magic. Whatever things were rare and precious were held to be good against disease—gold, amber, coral, pearls, and the dust of mummies; whatever took strange forms of life—toads, earthworms, and the like; whatever looked like the disease, after the doctrine of signatures—pulmonaria for the lungs, because the spots on its leaves were like tubercle, a kidney-shaped fruit for the kidneys, a heart-shaped fruit for the heart, and yellow carrots for the yellow jaundice. Among the drugs in the 1618 Pharmacopœia are *cranium humanum*, *mandibula lucii*, *nidus hirundinum*, *sericum crudum*, *linum vivum*, and *pilus salamandræ*. In the Pharmacopœia of 1677 are *exuviæ serpentis*, *telæ aranearum*, *saliva jejuni*, *cranium hominis violentâ morte extincti*, and worse obscenities.

Soon after the publication of this Pharmacopœia, on February 6, 1685, King Charles II. died; and in the Library of the Society of Antiquaries there is a manuscript account in Latin, by Dr. Scarbrugh, how the case was treated. The King had sixteen physicians, and nine consultations in five days; and to say "everything was done that was possible" gives no idea of the vigour of the treatment. Finally, the day he died, they gave him, eleven of them in consultation —*totus medicorum chorus ab omni spe destitutus*—they gave him, as *more generous cardiacs*, the *lapis Goæ* and the *Bezoar-stone*. The *lapis Goæ* was a dust of topaz, jacinth, sapphire, ruby, pearl, emerald, bezoar, coral, musk, ambegris, and gold, all made into a pill and polished; and the *bezoar* is a calculus found in the intestines of herbivorous animals. Half a century later, the Pharmacopœia of 1721 still included ants'-eggs, teeth, *lapis nephriticus*, and other horrors; and in the Pharmacopœia of 1746, though the dust or Egyptian mummies was ruled out, vipers and wood-lice were retained.

Certainly these "last enchantments of the Middle Ages" were slow to depart. Clinical observation, anatomy, and pathology, had all failed to bring about a right understanding of the actions of drugs. It was the physiologists, not the doctors, who first formulated the exact use of drugs; it was Bichat, Magendie, and Claude Bernard. That is the whole meaning of Magendie's work on the upas-poison and on strychnine, and Claude Bernard's work on curari and digitalis.

Of these four substances, two only are of any use in practice; yet Magendie's study of strychnine [1] was of immeasurable value, not so much because it gave the doctors a "more generous cardiac," though that was a great gift, but because it revealed the *selective* action of drugs. Contrast his account of strychnine with Ambroise Parè's story how they tested the bezoar-stone on the thief instead of hanging him; contrast Bernard's chapter on curari with Dr. Scarbrugh's notes on the King's death, with all the Crown jewels inside him: you are in two different worlds. The *selective* action of drugs—the affinity between strychnine and the central nerve-cells, between curari and the terminal filaments of the motor nerves—that was the revolutionary teaching of science: and it came, not by experience, but by experiment.

Take Prof. Fraser's address on "The Action of Remedies, and the Experimental Method," at the International Medical Congress in London, 1881:—

> "The introduction of this method is due to Bichat; and, by its subsequent application by Magendie, pharmacology was originated as the science we now recognise. Bichat represents a transition state, in which metaphysical conceptions were mingled with the results of experience. Magendie more clearly recognised the danger of adopting theories, in the existing imperfections of knowledge; and devoted himself to the supplementing of these imperfections by experiments on living animals. The advantages

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[1] For a full statement of the great value of this study of strychnine, see Cl. Bernard, *Leçons de Physiologie Opératoire*, 1879, p. 89.

of such experiments he early illustrated by his investigation on the upas-poison ; and afterwards by a research on the then newly discovered alkaloid, strychnia. . . . He demonstrated the action of this substance upon the spinal cord, by experiments upon the lower animals, so thoroughly, that subsequent investigations have added but little to his results."

Or take Professor Fraser's account of digitalis : —

"It was introduced as a remedy for dropsy ; and, on the applications which were made of it for the treatment of that disease, a slowing action upon the cardiac movements was observed, which led to its acquiring the reputation of a cardiac sedative. Numerous observations were made on man by the originators of its application, by Dr. Sanders and many other physicians, in which special attention was paid to its effects upon the circulation ; but no further light was thrown upon its remarkable properties, with the unimportant exception that in some cases it was found to excite the circulation. It was not until the experimental method was applied in its investigation, in the first instance by Claude Bernard, and subsequently by Dybkowsky, Pelikan, Meyer, Boehm, and Schmiedeberg, that the true action of digitalis upon the circulation was discovered. It was shown that the effects upon the circulation were not in any exact sense sedative, but, on the contrary, stimulant and tonic, rendering the action of the heart more powerful, and increasing the tension in the blood-vessels. The indications for its use in disease were thereby revolutionised, and at the same time rendered more exact ; and the striking benefits which are now afforded by the use of this substance in most (cardiac) diseases were made available to humanity."

Or take Dr. Lauder Brunton's account of the action of nitrite of amyl in angina pectoris :—

> "The action of nitrite of amyl in causing flushing was first observed by Guthrie, and Dr. B. W. Richardson recommended it as a remedy in spasmodic conditions, from the power he thought it to possess of paralysing motor nerves. In the spring of 1867 I had opportunities of constantly observing a patient who suffered from angina pectoris, and of obtaining from him numerous sphygmographic tracings, both during the attack and during the interval. These showed that during the attack the pulse became quicker, the blood-pressure rose, and the arterioles contracted. . . . It seemed probable that the great rise in tension was the cause of the pain, and it occurred to me that if it was possible to diminish the tension by drugs instead of by bleeding, the pain would be removed.
>
> "I knew from unpublished experiments on animals by Dr. A. Gamgee that nitrite of amyl had this power, and therefore tried it on the patient. My expectations were perfectly answered. The pain usually disappeared in three-quarters of a minute after the inhalation began, and at the same time the pulse became slower and much fuller, and the tension diminished."

Of course it would be easy to lengthen out the list. Aconite, belladonna, calcium chloride, colchicum, cocain, chloral, ergot, morphia, salicylic acid, strophanthus, the chief diuretics, the chief diaphoretics —all these drugs, and a host more, have been studied and learned by experiments on animals. Then comes the answer, that drugs act differently on animals and on men. The few instances, that give a wise air to this foolish answer, were known long ago to everybody: they do not so much as touch the facts of daily practice:—

> "The action of drugs on man differs from that on the lower animals chiefly in respect to the brain, which is so much more greatly developed in man. Where the structure of an organ or tissue is nearly the same in man and in the lower animals, the action of drugs upon it is similar. Thus we find that carbonic oxide, and nitrites, produce similar changes in the blood of frogs, dogs, and man, that curare paralyses the motor nerves alike in them all, and veratria exerts upon the muscles of each its peculiar stimulant and paralysing action. Where differences exist in the structure of the various organs, we find, as we would naturally expect, differences in their reaction to drugs. Thus the heart of the frog is simpler than that of dogs or men, and less affected by the central nervous system; we consequently find that while such a drug as digitalis has a somewhat similar action upon the hearts of frogs, dogs, and men, there are certain differences between its effect upon the heart of a frog and on that of mammals.
>
> "Belladonna offers another example of apparent difference in action—a considerable dose of belladonna will produce almost no apparent effect upon a rabbit, while a smaller dose in a dog or a man would cause the rapidity of the pulse to be nearly doubled. Yet in all three—rabbits, dogs, and men—belladonna paralyses the power of the vagus over the heart. The difference is that in rabbits the vagus normally exerts but little action on the heart, and the effect of its paralysis is consequently slight or hardly appreciable." (Prof. Fraser.)

It would be strange indeed, if experts who work in micromillimetres and decimal milligrammes, and study the vanishing-point of microscopic structures, and measure and ordain infinitesimal changes in invisible organisms, were blind to such gross and palpable differences as exist between men and pigeons in their susceptibility to a dose of opium.

Anæsthetics must be reckoned among the drugs that have been studied on animals: but, for the discovery of them, men experimented on themselves. The first use of nitrous oxide (laughing gas) in surgery was December 11, 1844, when Horace Wells, of Connecticut, had it administered to himself for the removal of a tooth. The first use of ether was made by Dr. Long, of Athens, Georgia; but he did not publish the case, or follow up the work: and the honour of the discovery of ether went to Morton, of Boston: who made repeated experiments, both on animals and on himself. The date when he first rendered himself absolutely unconscious for seven or eight minutes is September 30, 1846; and the first operation under ether was done on October 16th, in the Massachusetts General Hospital. The first use of chloroform was November 4, 1847, that famous evening when Simpson, George Keith, and Matthews Duncan took it together. The whole history of anæsthesia is to be found in the *Practitioner*, October, 1896.

It is sometimes said that the men who make experiments on animals ought to make them on themselves. But they do, hundreds of them, and suffer for it: Heaven knows the list is long enough—the discoverers of anæsthesia, Hunter, Garré, Koch, Klein, Moor, Haffkine, Grassi, Bochefontaine, Quesada, Sanarelli, Pettenkofer—these and many more, here or abroad, have done it, as part of the day's work; and some—by accidental infection, like Chabry and Villa, or by deliberate self-inoculation, like Carrion—have been killed:—

"Dr. Angelo Knorr, *Privat-docent* in the Veterinary School of Munich, died on February 22nd from acute glanders, contracted in the course of an experimental research on mallein. Helmann, the Russian investigator who discovered mallein, himself fell a victim to accidental inoculation of the glanders virus. Some time afterwards another Russian, Protopopow, died of glanders contracted in a French laboratory. An Austrian physician, Dr. Koffman-Wellenhof, died of the same disease, contracted in the Institute of Hygiene at Vienna. On January 17th of the present year Dr. Guiseppe Bosso, of the University of Turin, died of infection contracted in the course of cultivations of tubercle-bacilli made in his laboratory. Not long before, Dr. Lola, assistant in the maternity department of the Czech University Hospital of Prague, died of tetanus caused by an experimental inoculation made on himself. Some fourteen or fifteen years ago, a medical student of Lima proved that 'verruga Peruana' is an infectious disease by inoculating himself with it, an act of scientific devotion which cost him his life.[1]

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[1] Daniel Carrion, born 1859 at Cerro de Pasco, proved, by self-inoculation, the identity of the two forms of the disease, August 27,

> Besides those who have died, there are many who have only escaped with their lives after long and painful illness. Professor Kourloff contracted anthrax in a laboratory at Munich, and was saved only by vigorous surgery. Dr. Nicolas supplied, in his own person, the first example of tetanus produced in man by inoculation of the pure toxin of the bacillus of Nicolaier." (*Brit. Med. Journal*, March 18, 1899.)

These men—and the list might be made much longer—fell ill, or died, or killed themselves over laboratory work; and the deaths of Barisch, Dr. Müller, and Nurse Pecha from plague at Vienna (October, 1898), are a further instance that there is danger in the constant handling of cultures. But at Vienna there was also gross carelessness on the part of one man. In laboratories in all parts of the world there are stored cultures of all sorts of organisms, yet no harm comes of it. "More cases of infection occur amongst young medical men attending fever cases, whether in private practice or hospital wards, in a single month, than have occurred in the whole of the laboratories in the world since they were established." (*British Medical Journal*, October 29, 1898.) Outside the laboratory, outside the fever hospitals, the risk is something less than a negligible quantity:—

> "Apart from plague and cholera, in all the big laboratories studies are uninterruptedly pursued, from one end

1885; died of the disease, October 5th. See *Ann. de l'Inst. Past.*, Sept., 1898.

of the year to the other, upon anthrax, glanders, influenza, Malta fever, various tropical diseases which do not exist at all or are rare in the countries where they are being studied. The laboratories in question are situated in the largest and most important towns of their respective countries; and, within those towns, very often in the most fashionable or most populous centres. . . . On no occasion was there even a suspicion aroused of an epidemic having been produced by any of the above-mentioned institutes, or by those tens of thousands of operations against cholera performed in India." (Haffkine, *Madras Mail*, December 8, 1898.)

XV

SNAKE-VENOM

THE Report of the 1875 Commission said—

> "It is not possible for us to recommend that the Indian Government should be prohibited from pursuing its endeavours to discover an antidote for snake-bites; or that, without such an effort, your Majesty's Indian subjects should be left to perish in large numbers annually from the effects of these poisons."

Certainly it was not possible; and the numbers are large indeed. During 1897, 4,227 persons were killed by wild animals in India, and 20,959 by snakes. (*British Medical Journal*, November 5, 1898.)

Sir Joseph Fayrer's name must be put in the highest place of all those who have studied the venomous snakes of India.

Sewall, in 1887, showed that animals could be rendered immune, by repeated inoculation with minute quantities of rattlesnake-venom, to a dose seven times as large as would kill an unprotected animal. Kanthack, in 1891, immunised animals in the same way against cobra-venom. He also made experiments to ascertain whether the blood-serum of these animals acted as an antidote to the venom. Then came the work of Calmette, Fraser,[1] Phisalix, Bertrand, Martin (Australia), Stephens, and Meyers. The results obtained by Calmette are a good instance of the fineness and accuracy of the experimental method. It is to be noted that the animals were inoculated with a fine needle, not thrust into cages with snakes, as at zoological gardens; and that an animal thus poisoned has a painless death. The different venoms were measured in decimal milligrammes, and their potency was estimated according to the body-weight of the animal inoculated. As with tetanus, so with snake-venom, there must be a standard, or "unit of toxicity":—

> "The following table gives the relative toxicity, for 1 kilogr. of rabbit, of the different venoms that I have tested. To denote this toxicity I use terms such as Behring, Roux, and Vaillard used for the toxin of tetanus, taking the number of grammes of animal killed by one gramme of toxin:
>
> 1. Venom of *naja*......0·25 mgr. per kilogr. of rabbit. One gramme of this venom kills 4,000 kilogrammes of rabbit; it has, therefore, an activity of 4,000,000

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[1] Professor Fraser's observations on the antidotal properties of the bile are, of course, of the utmost importance; not only in preventive medicine, but also in physiology.

2. Venom of *hoplocephalus*	0·29 mgr.	3,450,000
3. Venom of *pseudechis*	1·25 mgr.	800,000
4. Venom of *pelias berus*	4·00 mgr.	250,000

"Of course, this estimation of virulence is not absolute; it varies considerably according to the species of animal tested. Thus the guinea-pig, and still more the rat, are extremely sensitive. For instance, 0·15 mgr. of viper-venom is enough to kill, in less than 12 hours, 500 grammes of guinea-pig; so that the activity of this venom with a guinea-pig is 3,333,000, but with a rabbit is not more than 650,000. With more resistent animals, the opposite result is obtained: about 10 mgr. of cobra-venom are necessary to kill a dog of 6·50 kilogrm. weight; but to kill the same weight of rabbit 1·65 mgr. is enough. Thus the virulence of this venom with the rabbit is 4,000,000; but with the dog not more than 650,000."

By experiments in test-tubes, Calmette studied these venoms under the influences of heat and various chemical agents. He found how to attenuate their virulence, and how to diminish the local inflammation round the point of inoculation; and it was in the course of these test-tube experiments and inoculations that he discovered the value of calcium hypochlorite as a local application. Working, by various methods, with attenuated venoms, he was able to immunise animals:—

"I have come to immunise rabbits against quantities of venom that are truly colossal. I have got several, vaccinated more than a year ago, which take, without the least discomfort, so much as 40 mgr. of venom *naja tripudians* at a single injection ; that is to say, eno to kill 80 rabbits of 2 kilogr. weight, or 5 dogs.

"Five drops of serum from these rabbits wh neutralise *in vitro* (in a glass test-tube) the toxicity 1 mgr. of *naja* venom."

By 1894 he had found that the serum of an anin thus immunised by graduated doses of one kind venom, neutralised other kinds of venom :—

"If 1 mgr. of cobra-venom, or 4 mgr. of viper-ven be mixed, in a test-tube, with a small quantity of ser from an immunised rabbit, and a fresh rabbit be inocula with this mixture, it does not suffer any discomfort. I not even necessary that the serum should come from animal vaccinated against the same sort of venom as t in the mixture. *The serum of a rabbit immunised against venom of the cobra or the viper acts indifferently on all venoms that I have tested.*"

In 1894 he had prepared enough serum for treatment to be tried by his own countrymen practisi in some of the French colonies. In April, 1895, gave the following account of his work :—

"I have immunised two asses, one having recei 220 mgr. of *naja*-venom from September 25 to Deceml 31, 1894, and the other 160 mgr. from October 15 December 31. The serum of the first of these t animals has now reached this point, that half a cul centimetre destroys the toxicity of 1 mgr. of *naja*-veno Four cubic centimetres of this serum, injected four ho before the inoculation of a dose of venom enough to

> twice over, preserve the animal in every case. It is also therapeutic, under the conditions that I have already defined; that is to say, if you first inoculate a rabbit with such a dose of venom as kills the control-animals in three hours, and then, an hour after injecting the venom, inject under the skin of the abdomen 4 to 5 cubic centimetres of serum, recovery is the rule. When you interfere later than this the results are uncertain; and in all my experiments the delay of an hour and a half is the most that I have been able to reach.
>
> "This antivenomous serum of asses has these same antitoxic properties with all kinds of snake-venom; it is equally active *in vitro*, preventive, and therapeutic, with the venoms of *cerastes*, of *trigonocephalus*, of *crotalus*, and of four kinds of Australian snakes that Mr. MacGarvie Smith has sent to M. Roux. I am still injecting these two animals with venom, and I hope to give to their serum at last a much greater antitoxic power."

In 1896 four successful cases of this treatment in the human subject were reported in the *British Medical Journal*. In 1898 Calmette made the following statement of his results:—

> "It is now nearly two years since the use of my antivenomous serum was introduced in India, in Algeria, in Egypt, on the West Coast of Africa, in America, in the West Indies, Antilles, &c. It has been very often used for men and domestic animals (dogs, horses, oxen), and up to now none of those that have received an injection of serum have succumbed. . . . A great number of observations have been communicated to me, and not one of them refers to a case of failure." (*British Medical Journal*, May 14, 1898.)

NOTE.

For an excellent account of Fraser's and Calmette's work, and of its use in practice, see Dr. Stone's paper in the *Boston Medical and Surgical Journal*, April 7, 1898.

From all these instances in physiology, pathology, bacteriology, and therapeutics, we come to consider the Act relating to experiments on animals in this country. Nothing has been said about the bacteriology of pneumonia, influenza, cerebro-spinal meningitis, and certain other diseases. Nothing has been said of the many inventions of medical and surgical practice that owe something, but not everything, to experiments on animals. Artificial respiration, the transfusion of saline fluid, the hypodermic administration of drugs, the use of oxygen for inhalation, the torsion of arteries, the grafting of skin, the transplantation of bone, the absorbable ligature, the diagnostic and therapeutic uses of electricity, the rational employment of blood-letting—all these good methods have been left out of the list; only some facts have been presented, those that mark most clearly the advance of knowledge and of practice, and stand up even above the rest of the work. There they will stand, when we are all dead and gone: and by them, as by landmarks, all further advance will be guided.

THE ACT RELATING TO EXPERIMENTS ON ANIMALS

ACT 39 AND 40 VIC. c. 77

THE Royal Commission, on the Practice of subjecting Live Animals to Experiments for Scientific Purposes, was appointed on June 22, 1875: Lord Cardwell (chairman), Lord Winmarleigh, Mr. W. E. Forster, Sir John Karslake, Mr. Huxley, Mr. Erichsen, and Mr. Hutton. Between July 5th and December 20th, fifty-three witnesses were examined, and 6,551 question were put and answered. The Report bears date January 8, 1876, and in that year the present Act received the Royal Assent.

In 1876 the doctrine of spontaneous generation was preached for the last time in England: and bacteriology was just beginning to be taught. The evidence before the Commission is all or nearly all of it about physiology—Magendie, Claude Bernard, Sir Charles Bell: the action of curare, the *Handbook for the Physiological Laboratory*. Very little is said of pathology; and of bacteriology hardly a word. Practically, physiology alone came before the Commissioners; and such experiments in physiology as are now, the youngest of them, a quarter of a century old. Even the *Zoophilist* advises its lecturers to cease from profaning these venerable relics of 1875 :—

> "An old lecture or address must, to a certain extent, be always a perfunctory performance. The Blue Book has long been a valuable mine for our speakers, but it is getting exhausted now. Sir William Fergusson was, no doubt, a great authority on our side, but he carries no weight with our present-day medical students. . . . The recital of the horrors of Magendie's, Mantegazza's, and Schiff's laboratories have little or no good effect on English audiences ; they are set aside as foreign and out-of-date. . . . How often have we heard of the horrible experiments of Dr. Brachet. . . . But Dr. Brachet was born in 1789 and died in 1858, and in France too." (*Zoophilist*, February 1, 1899.)

At the time of the passing of the Act, bacteriology had hardly made a beginning. Therefore the Act made no special provision for inoculations, injections, and the whole study of immunisation of animals and men against disease. Experiments of this kind have to be scheduled under one of the existing Certificates, to bring them under an Act that was drafted without foreknowledge of them. Certificate A and Certificate B have to be used for this purpose :—

Certificate A.

> "We hereby certify that, in our opinion, insensibility in the animal on which any such experiment may be performed cannot be produced by anæsthetics without necessarily frustrating the object of such experiments."

Certificate B.

"We hereby certify that, in our opinion, the killing of the animal on which any such experiment is performed before it recovers from the anæsthetic administered to it, would necessarily frustrate the object of such experiment."

Under one or other of these Certificates must be scheduled all inoculations, injections, feeding-experiments, transplantations of particles of disease, immunisations, and the like. They must be scheduled somehow; and that is the only way of doing it. Where the act of inducing the disease would itself give any pain, if an anæsthetic were not administered—as in the subdural inoculation of a rabbit, or the intra-peritoneal inoculation of an animal with a particle of cancerous tissue—there the licensee must hold, together with his license, Certificate B, because the act of inducing the disease is itself an operation, done under an anæsthetic. If the animal be a dog or a cat, he must hold Certificates B and EE; if it be a horse, ass, or mule, Certificates B and F.

Where the act of inducing the disease is not itself painful—as in ordinary inoculation, and in feeding-experiments—the licensee must hold, together with his license, Certificate A, because the animal is not anæsthetised; it is not a painful operation; the experiment consists not in the act of putting the hypodermic needle under the animal's skin, but in the subsequent observation of the course of the disease. Take, for instance, the inoculation of a guinea-pig with tubercle-bacilli: the experiment is the production of tubercle; the experiment lasts till the animal is killed and found to be infected; it is therefore scheduled under Certificate A. Or take the testing, on an animal, of an antitoxin: the experiment is not the injection, but the observation of the result; the animal may not suffer, but the injection must still be done under Certificate A. And, if the animal be a dog or a cat, the licensee must hold Certificates A and E; or, if it be a horse, ass, or mule, Certificates A and F.

This want of a special certificate for inoculations is an important matter, because it has led to the belief that painful operations are performed, without anæsthesia, in cases where the only instrument used is a needle. It is hardly reasonable, for instance, that the inoculation of a mouse should be scheduled as a painful operation performed without anæsthesia. The disease, thus painlessly induced, may in many cases be called painless; for instance, tuberculosis in the guinea-pig, snake-venom in the rat, septicæmia in the mouse, malaria in small birds. In other cases, there are such pain and fever as are part of the disease. The form that rabies takes in rabbits may fairly be called painless. Inoculations not under the skin, but into the anterior chamber of the eye, are very seldom made; they sound cruel, but cocain renders the surface of the eye wholly insensitive, and the anterior chamber is so far insensitive that a man with blood or pus (*hypopyon*) in the anterior chamber of the eye may suffer no pain from it. A horse or an ass kept for the giving of an antitoxic serum has a more comfortable life than an omnibus horse; and this preparation of the antitoxins, since it is not an experiment, but a direct use of animals in the recognised service of man, does not require a license or certificates under the Act. But the testing of an antitoxin is an experiment, and must be made under a license and Certificate A.

It is not the business of this book to consider whether the sensitiveness of a dog, a rabbit, or a guinea-pig can fairly be stated in terms of the physical and mental sensitiveness of men and women. In the world of animals, as in the world of humanity, there are differences of sensitiveness. Anyhow, the pain inflicted on animals may in some cases be measured:—

> "A guinea-pig that will rest quietly in your hands before you commence to inject it will remain perfectly quiet during the introduction of the needle under the skin; and the moment it is returned to the cage it resumes its interrupted feeding.
>
> "Arteries, veins, and most of the parts of the viscera are in the same way (as the heart)[1] without the sense of touch. We have actual proof of this in what takes place when a horse is bled for the purpose of obtaining curative serum. With a sharp lance a cut may be made in the skin so quickly and easily that the animal does nothing more than twitch the skin-muscle of the neck, or give his head a

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[1] The reference is to the famous case showed by Harvey to King Charles I., where the heart was exposed almost naked through an opening in the chest, and was found insensitive. See Power's *Life of Harvey*, p. 246.

shake, whilst of the further proceeding of introducing a hollow needle into the vein the animal takes not the slightest notice. Some horses, indeed, will stand perfectly quiet during the whole operation, munching a carrot, nibbling at a wisp of hay, or playing with a button on the vest of the groom standing at its head.

"Harrowing details concerning the horrors of trephining rabbits for Pasteur's antirabic treatment are frequently supplied for popular consumption, but how little real existence any suffering in connection with the operation has may be gathered from the fact that if, as a preliminary measure, the skin be benumbed with carbolic acid, the whole operation, from making the incision through the skin to cutting out the piece of bone with a fine trephine and passing a needle under the dura mater, may be done without once causing the animal to withdraw its attention from the important business of munching a bit of cabbage-leaf or a scrap of succulent carrot." (Woodhead, *Medical Magazine*, June, 1898.)

It will be best to put here (1) the full text of the Act, (2) an account of the anæsthetics used for animals, (3) the Reports of the Government Inspector for England and Scotland, from 1896 to 1898 inclusive, (4) various official statements.

I.

AN ACT TO AMEND THE LAW RELATING TO CRUELTY TO ANIMALS. [15th August, 1876.]

WHEREAS it is expedient to amend the law relating to cruelty to animals by extending it to the cases of animals which for medical, physiological, or other scientific purposes are subjected when alive to experiments calculated to inflict pain :

Be it enacted by the Queen's most Excellent Majesty, by and with the advice and consent of the Lords Spiritual and Temporal, and Commons, in this present Parliament assembled, and by the authority of the same, as follows :

Short title.

1. This Act may be cited for all purposes as "The Cruelty to Animals Act, 1876."

Prohibition of painful experiments on animals.

2. A person shall not perform on a living animal any experiment calculated to give pain, except subject to the restrictions imposed by this Act. Any person performing or taking part in performing any experiment calculated to give pain, in contravention of this Act, shall be guilty of an offence against this Act, and shall, if it be the first offence, be liable to a penalty not exceeding fifty pounds, and if it be the second or any subsequent offence, be liable, at the discretion of the court by which he is tried, to a penalty not exceeding one hundred pounds or to imprisonment for a period not exceeding three months.

General restrictions as to performance of painful experiments on animals.

3. The following restrictions are imposed by this Act with respect to the performance on any living animal of an experiment calculated to give pain ; that is to say,

(1) The experiment must be performed with a view to the advancement by new discovery of physiological knowledge or of knowledge which will be useful for saving or prolonging life or alleviating suffering ; and

(2) The experiment must be performed by a person holding such license from one of Her Majesty's Principal Secretaries of State, in this Act referred to as the Secretary of State, as is in this Act mentioned, and in the case of a person holding such conditional license as is hereinafter mentioned, or of experiments performed for the purpose of instruction in a registered place ; and

(3) The animal must during the whole of the exper ment be under the influence of some anæsthet of sufficient power to prevent the animal feeli pain ; and

(4) The animal must, if the pain is likely to contin after the effect of the anæsthetic has ceased, if any serious injury has been inflicted on t animal, be killed before it recovers from t influence of the anæsthetic which has bee administered ; and

(5) The experiment shall not be performed as an illu tration of lectures in medical schools, hospital colleges, or elsewhere ; and

(6) The experiment shall not be performed for th purpose of attaining manual skill.

Provided as follows ; that is to say,

(1) Experiments may be performed under the foregoin provisions as to the use of anæsthetics by person giving illustrations of lectures in medic schools, hospitals, or colleges, or elsewhere, o such certificate being given as in this Ac mentioned, that the proposed experiments ar absolutely necessary for the due instruction o the persons to whom such lectures are give with a view to their acquiring physiologic knowledge or knowledge which will be useful t them for saving or prolonging life or alleviatin suffering ; and

(2) Experiments may be performed without anæsthetic on such certificate being given as in this Ac mentioned that insensibility cannot be produce without necessarily frustrating the object o such experiments ; and

(3) Experiments may be performed without the perso who performed such experiments being under a

obligation to cause the animal on which any such experiment is performed to be killed before it recovers from the influence of the anæsthetic on such certificate being given as in this Act mentioned, that the so killing the animal would necessarily frustrate the object of the experiment, and provided that the animal be killed as soon as such object has been attained; and

(4) Experiments may be performed not directly for the advancement by new discovery of physiological knowledge, or of knowledge which will be useful for saving or prolonging life or alleviating suffering, but for the purpose of testing a particular former discovery alleged to have been made for the advancement of such knowledge as last aforesaid, on such certificate being given as is in this Act mentioned that such testing is absolutely necessary for the effectual advancement of such knowledge.

Use of urari as an anæsthetic prohibited.

4. The substance known as urari or curare shall not for the purposes of this Act be deemed to be an anæsthetic.

Special restrictions on painful experiments on dogs, cats, &c.

5. Notwithstanding anything in this Act contained, an experiment calculated to give pain shall not be performed without anæsthetics on a dog or cat, except on such certificate being given as in this Act mentioned, stating, in addition to the statements hereinbefore required to be made in such certificate, that for reasons specified in the certificate the object of the experiment will be necessarily frustrated unless it is performed on an animal similar in constitution and habits to a cat or dog, and no other animal is available for such experiment; and an experiment calculated to give pain shall not be performed on any horse, ass, or mule except on such certificate being given as in this Act mentioned that the object of the experiment will be necessarily frustrated unless it is performed on a horse, ass, or mule, and that no other animal is available for such experiment.

Absolute prohibition of public exhibition of painful experiments.

6. Any exhibition to the general public, whether admitted on payment of money or gratuitously, of experiments on living animals calculated to give pain shall be illegal.

Any person performing or aiding in performing such experiments shall be deemed to be guilty of an offence against this Act, and shall, if it be the first offence, be liable to a penalty not exceeding fifty pounds, and if it be the second or any subsequent offence be liable at the discretion of the court by which he is tried, to a penalty not exceeding one hundred pounds or to imprisonment for a period not exceeding three months.

And any person publishing any notice of any such intended exhibition by advertisement in a newspaper, placard, or otherwise shall be liable to a penalty not exceeding one pound.

A person punished for an offence under this section shall not for the same offence be punishable under any other section of this Act.

Administration of Law.

Registry of place for performance of experiments.

7. The Secretary of State may insert, as a condition of granting any license, a provision in such license that the place in which any experiment is to be performed by the licensee is to be registered in such manner as the Secretary of State may from time to time by any general or special order direct; provided that every place for the performance of experiments for the purpose of instruction under this Act shall be approved by the Secretary of State, and shall be registered in such manner as he may from time to time by any general or special order direct.

8. The Secretary of State may license any person whom he may think qualified to hold a license to perform experiments under this Act. A license granted by him may be for such time as he may think fit, and may be revoked by him on his being satisfied that such license ought to be revoked. There may be annexed to such license any conditions which the Secretary of State may think expedient for the purpose of better carrying into effect the objects of this Act, but not inconsistent with the provisions thereof.

License by Secretary of State.

9. The Secretary of State may direct any person performing experiments under this Act from time to time to make such reports to him of the result of such experiments, in such form and with such details as he may require.

Reports to Secretary of State.

10. The Secretary of State shall cause all registered places to be from time to time visited by inspectors for the purpose of securing a compliance with the provisions of this Act, and the Secretary of State may, with the assent of the Treasury as to number, appoint any special inspectors, or may from time to time assign the duties of any such inspectors to such officers in the employment of the Government, who may be willing to accept the same, as he may think fit, either permanently or temporarily.

Inspection by Secretary of State.

11. Any application for a license under this Act and a certificate given as in this Act mentioned must be signed by one or more of the following persons—that is to say,

Certificate of scientific bodies for exceptions to general regulations.

The President of the Royal Society;
The President of the Royal Society of Edinburgh;
The President of the Royal Irish Academy;
The Presidents of the Royal College of Surgeons in London, Edinburgh, or Dublin;
The Presidents of the Royal College of Physicians in London, Edinburgh, or Dublin;
The President of the General Medical Council;

- The President of the Faculty of Physicians and Surgeons of Glasgow ;
- The President of the Royal College of Veterinary Surgeons, or the President of the Royal Veterinary College, London, but in the case only of an experiment to be performed under anæsthetics with a view to the advancement by new discovery of veterinary science ;

and also (unless the applicant be a professor of physiology, medicine, anatomy, medical jurisprudence, materia medica, or surgery in a university in Great Britain or Ireland, or in University College, London, or in a college in Great Britain or Ireland, incorporated by royal charter) by a professor of physiology, medicine, anatomy, medical jurisprudence, materia medica, or surgery in a university in Great Britain or Ireland, or in University College, London, or in a college in Great Britain or Ireland, incorporated by royal charter.

Provided that where any person applying for a certificate under this Act is himself one of the persons authorised to sign such certificate, the signature of some other of such persons shall be substituted for the signature of the applicant.

A certificate under this section may be given for such time or for such series of experiments as the person or persons signing the certificate may think expedient.

A copy of any certificate under this section shall be forwarded by the applicant to the Secretary of State, but shall not be available until one week after a copy has been so forwarded.

The Secretary of State may at any time disallow or suspend any certificate given under this section.

Power of judge to grant license for experiment when necessary in criminal

12. The powers conferred by this Act of granting license or giving a certificate for the performance experiments on living animals may be exercised by order in writing under the hand of any judge of the High Court of Justice in England, of the High Court of Session in Scotland, or of any of the superior courts in Ireland, including any court to which the jurisdiction of such last-mentioned courts may be transferred, in a case where such judge is satisfied that it is essential for the purposes of justice in a criminal case to make any such experiment.

Legal Proceedings.

Entry on warrant by justice.

13. A justice of the peace, on information on oath that there is reasonable ground to believe that experiments in contravention of this Act are being performed by an unlicensed person in any place not registered under this Act may issue his warrant authorising any officer or constable of police to enter and search such place, and to take the names and addresses of the persons found therein.

Any person who refuses admission on demand to a police officer or constable so authorised, or obstructs such officer or constable in the execution of his duty under this section, or who refuses on demand to disclose his name or address, or gives a false name or address, shall be liable to a penalty not exceeding five pounds.

Prosecution of offences and recovery of penalties in England.

14. In England, offences against this Act may be prosecuted and penalties under this Act recovered before a court of summary jurisdiction in manner directed by the Summary Jurisdiction Act.

In England "Summary Jurisdiction Act" means the Act of the session of the eleventh and twelfth years of the reign of Her present Majesty, chapter forty-three, intituled "An Act to facilitate the performance of the duties of justices of the peace out of sessions within England and Wales with respect to summary convictions and orders," and any Act amending the same.

"Court of summary jurisdiction."

"Court of summary jurisdiction" means and includes any justice or justices of the peace, metropolitan police magistrate, stipendiary or other magistrate, or officer, by whatever name called, exercising jurisdiction in pursuance of the Summary Jurisdiction Act: Provided that the court when hearing and determining an information under this Act shall be constituted either of two or more justices of the peace in petty sessions, sitting at a place appointed for holding petty sessions, or of some magistrate or officer sitting alone or with others at some court or other place appointed for the administration of justice, and for the time being empowered by law to do alone any act authorised to be done by more than one justice of the peace.

Power of offender in England to elect to be tried on indictment, and not by summary jurisdiction.

15. In England, where a person is accused before a court of summary jurisdiction of any offence against this Act in respect of which a penalty of more than five pounds can be imposed, the accused may, on appearing before the court of summary jurisdiction, declare that he objects to being tried for such offence by a court of summary jurisdiction, and thereupon the court of summary jurisdiction may deal with the case in all respects as if the accused were charged with an indictable offence and not an offence punishable on summary conviction, and the offence may be prosecuted on indictment accordingly.

Form of appeal to quarter sessions.

16. In England, if any party thinks himself aggrieved by any conviction made by a court of summary jurisdiction on determining any information under this Act, the party so aggrieved may appeal therefrom, subject to the conditions and regulations following:

(1) The appeal shall be made to the next court of general or quarter sessions for the county or place in which the cause of appeal has arisen, holden not less than twenty-one days after the

decision of the court from which the appeal is made ; and

(2) The appellant shall, within ten days after the cause of appeal has arisen, give notice to the other party and to the court of summary jurisdiction of his intention to appeal, and of the ground thereof; and

(3) The appellant shall, within three days after such notice, enter into a recognisance before a justice of the peace, with two sufficient sureties, conditioned personally to try such appeal, and to abide the judgment of the court thereon, and to pay such costs as may be awarded by the court, or give such other security by deposit of money or otherwise as the justice may allow ; and

(4) Where the appellant is in custody the justice may, if he think fit, on the appellant entering into such recognisance or giving such other security as aforesaid, release him from custody ; and

(5) The court of appeal may adjourn the appeal, and upon the hearing thereof they may confirm, reverse, or modify the decision of the court of summary jurisdiction, or remit the matter to the court of summary jurisdiction with the opinion of the court of appeal thereon, or make such other order in the matter as the court thinks just, and if the matter be remitted to the court of summary jurisdiction the said last-mentioned court shall thereupon re-hear and decide the information in accordance with the order of the said court of appeal. The court of appeal may also make such order as to costs to be paid by either party as the court thinks just.

Prosecution of offences and recovery of penalties in Scotland.

17. In Scotland, offences against this Act may be prosecuted and penalties under this Act recovered under the provisions of the Summary Procedure Act, 1864, or if a person accused of any offence against this Act in respect of which a penalty of more than five pounds can be imposed, on appearing before a court of summary jurisdiction, declare that he objects to being tried for such offence in the court of summary jurisdiction, proceedings may be taken against him on indictment in the Court of Justiciary in Edinburgh or on circuit.

Every person found liable in any penalty or costs shall be liable in default of immediate payment to imprisonment for a term not exceeding three months, or until such penalty or costs are sooner paid.

Prosecution of offences and recovery of penalties in Ireland.

18. In Ireland, offences against this Act may be prosecuted and penalties under this Act recovered in a summary manner, subject and according to the provisions with respect to the prosecution of offences, the recovery of penalties, and to appeal of the Petty Sessions (Ireland) Act, 1851, and any Act amending the same, and in Dublin of the Acts regulating the powers of justices of the peace or of the police of Dublin metropolis. All penalties recovered under this Act shall be applied in manner directed by the Fines (Ireland) Act, 1871, and any Act amending the same.

Power of offender in Ireland to elect to be tried on indictment, and not by summary jurisdiction.

19. In Ireland, where a person is accused before a court of summary jurisdiction of any offence against this Act in respect of which a penalty of more than five pounds can be imposed, the accused may, on appearing before the court of summary jurisdiction, declare that he objects to being tried for such offence by a court of summary jurisdiction, and thereupon the court of summary jurisdiction may deal with the case in all respects as if the accused were charged with an indictable offence, and not an offence punishable on summary conviction, and the offence may be prosecuted on indictment accordingly.

Interpretation of "the Secretary of State" as to Ireland.

20. In the application of this Act to Ireland the term "the Secretary of State" shall be construed to mean the Chief Secretary to the Lord Lieutenant of Ireland for the time being.

Prosecution only with leave of Secretary of State.

21. A prosecution under this Act against a licensed person shall not be instituted except with the assent in writing of the Secretary of State.

Not to apply to invertebrate animals.

22. This Act shall not apply to invertebrate animals.

EXPERIMENTS ON ANIMALS

APPLICATION FOR LICENSE.

Address ____________________

Date ____________________

To the Right Honourable the Secretary of State for the Home Department.

SIR,

I * ____________________

____

____

beg to apply under the above-mentioned Act for a License for the performance of experiments on animals.

The place in which it is proposed that the experiments are to be performed is † ____________________

The experiments which it is proposed to perform are ‡

____

____

____

____

This application is supported by the recommendations appearing below.

I am,

SIR,

Your obedient Servant,

§ ____________________

We recommend that the above application be granted.

1. ‖ ____________________

¶ ____________________

** ____________________

2. ‖ ____________________

¶ ____________________

** ____________________

*** Here insert name and profession (see sec. 11 of Act) of applicant.**

† Here insert registered place. If the place is not registered it will be necessary for the person having authority over the building to apply to the Secretary of State for its registration.

‡ Here insert a general description of proposed experiments and their object; also state, if that is the case, the intention of applicant to send in a certificate or certificates (describing each certificate by its appropriate letter) with reference to the same experiments, or any other circumstances that may be material.

§ Here applicant to sign his name.

‖ Here the person recommending is to sign his name.

¶ Here state profession.

**** Here specify statutory qualification. (See sec. 11.)**

ACT 39 AND 40 VIC. c. 77

APPLICATION FOR REGISTRATION.

SIR,

beg to apply that

The application must be made by or on behalf of the person or persons having authority to dispose of the use of the building.

may be registered for the performance therein of experiments under the Act 39 & 40 Vict., c. 77.

The building must be named or described so that it can be identified.

SIR,
Your obedient Servant,

The Under-Secretary of State,
Home Department.

EXPERIMENTS ON ANIMALS

CERTIFICATE A.

* Here insert name, address, and profession of person to whom certificate is to be given.

WHEREAS*

of

† Here insert name, address, and statutory qualification of each person certifying.

has represented to us †

that he proposes, if duly authorised under the above-mentioned Act, to perform on living animals certain experiments described below : We hereby certify that, in our opinion, insensibility in the animal on which any such experiment may be performed cannot be produced by anæsthetics without necessarily frustrating the object of such experiment.

This certificate will not be in force after the day of or after the completion of experiments.

If it be desired that the certificate should either operate beyond two years, or should contain no limit as to the number of experiments, it will be advisable that the applicant for the certificate should communicate beforehand with the Secretary of State.

Signatures of Certifiers } †
to be attached here }

Date

Description of proposed experiments.

ACT 39 AND 40 VIC. c. 77

CERTIFICATE B.

WHEREAS*

of

* Here insert name, address, and profession of person to whom certificate is to be given.

has represented to us †

† Here insert name, address, and statutory qualification of each person certifying.

that he proposes, if duly authorised under the above-mentioned Act, to perform on living animals certain experiments described below, such animals being, during the whole of such experiments, under the influence of some anæsthetic of sufficient power to prevent their feeling pain: We hereby certify that, in our opinion, the killing of the animal on which any such experiment is performed before it recovers from the influence of the anæsthetic administered to it would necessarily frustrate the object of such experiment.

This Certificate will not be in force after the day of , or after the completion of experiments.

Signatures of Certifiers }
to be attached here } †

Date

If it be desired that the certificate should either operate beyond two years, or should contain no limit as to the number of experiments, it will be advisable that the applicant for the certificate should communicate beforehand with the Secretary of State.

Description of proposed experiments.

EXPERIMENTS ON ANIMALS

CERTIFICATE C.

* Here insert name, address, and profession of person to whom certificate is to be given. (Sec. 11 of Act.)

WHEREAS*

of

† Here insert name, address, and statutory qualification of each person certifying. (Sec. 11 of Act.

has represented to us †

that he proposes, if duly authorised under the above-mentioned Act, to perform at

by way of illustration of lectures to be there delivered, certain experiments described below on living animals, such experiments being performed under the provisions contained in the said Act as to the use of anæsthetics; We hereby certify that, in our opinion, the proposed experiments are absolutely necessary for the due instruction of persons to whom such lectures are to be given, with a view to their acquiring physiological knowledge, or knowledge which will be useful to them for saving or prolonging life or alleviating suffering.

This Certificate shall be in force so long as the holder is in possession of a license under the said Act.

Date

Description of proposed experiments.

ACT 39 AND 40 VIC. c. 77

CERTIFICATE D.[1]

WHEREAS*

* Here insert name, address, and profession of person to whom certificate is to be given. (Sec. 11 of Act.)

of

has represented to us†

† Here insert name, address, and statutory qualification of each person certifying. (Sec. 11 of Act.)

that he proposes, if duly authorised under the above-mentioned Act, to perform on living animals certain experiments described below, for the purpose of testing the former discoveries described below, alleged to have been made for the advancement of physiological knowledge, or knowledge which will be useful for saving or prolonging life or alleviating suffering: We hereby certify that, in our opinion, such testing is absolutely necessary for the effectual advancement of such knowledge.

This Certificate shall be in force until the day of , and no longer.

Date

Description of proposed experiments.	Description of former discoveries for the purpose of testing which the proposed experiments are to be made.

[1] This Certificate has fallen into disuse.

EXPERIMENTS ON ANIMALS

Certificate E.[1]

* Here insert name, address, and profession of person to whom certificate is to be given. (Sec. 11 of Act.)

WHEREAS*

of

† Here insert name, address, and statutory qualification of each person certifying. (Sec. 11 of Act.)

has represented to us †

that he proposes, if duly authorised under the abovementioned Act, to perform on dogs and cats, the experiments described below without anæsthetics : We hereby certify that, in our opinion, for the reasons specified below, the object of any such experiment will be necessarily frustrated, unless it is performed on an animal similar in constitution and habits to a dog or cat, and that no other animal is available for any such experiment.

This Certificate shall be in force until the day of , and no longer.

Date

Description of experiments to be performed.

Reasons why the object of any such experiment will be necessarily frustrated unless it is performed on an animal similar in constitution and habits to a dog or cat, and why no other animal is available for any such experiment.

---

[1] Certificate EE has been introduced, since the Act was passed to go with Certificate B, as Certificate E goes with Certificate A.

ACT 39 AND 40 VIC. c. 77

CERTIFICATE F.

WHEREAS*

of

* Here insert name, address, and profession of person to whom certificate is to be given. (Sec. 11 of Act.)

has represented to us†

† Here insert name, address, and statutory qualification of each person certifying. (Sec. 11 of Act.)

that he proposes, if duly authorised under the above-mentioned Act, to perform on horses, asses, or mules, the experiments described below : We hereby certify that, in our opinion, for the reasons specified below, the object of any such experiment will be necessarily frustrated, unless it is performed on a horse, ass, or mule, and that no other animal is available for such experiment.

This Certificate shall be in force until the day of , and no longer.

Date

Description of experiments to be performed.

Reasons why the object of any such experiment will be necessarily frustrated unless it is performed on a horse, ass, or mule, and why no other animal is available for any such experiment.

EXPERIMENTS ON ANIMALS

II

ANÆSTHETICS USED FOR ANIMALS

In almost every case, the anæsthetic used is chloroform or ether, sometimes combined with and followed by morphia or chloral. The nature of the anæsthetic used in each case must, of course, be stated in the returns sent to the Home Office. Of the use of ether, it need only be said that animals take it well, and that there is no difficulty in rendering them unconscious with it.

With some animals chloroform is equally good; with others it is dangerous to life. But Prof. Hobday, of the Royal Veterinary College, has lately published an account of five hundred administrations of chloroform to dogs, for the operations of veterinary surgery, with only one death. (*Lancet*, September, 1898.) Still, for dogs and cats, ether is used in preference to chloroform. Other animals take chloroform well.[1] And it is wholly false to say that "just a whiff" of chloroform or ether is given, or "just enough to keep the animal quiet." Lately, in an account of some experiments, it was stated that in two or three cases the anæsthesia was incomplete. Such use of chloroform or ether may be made, for good reasons, in certain surgical procedures, or for the alleviation of the pains of childbirth: but alike in surgery and in experiments on animals it is altogether exceptional, or something more than exceptional.

---

[1] The *Veterinary Record* lately published an excellent paper by Mr. Tasker on the best method of administering chloroform to horses; and the *Lancet*, February 18, 1899, says, in a review of it, "We fear that much unnecessary suffering to animals has in the past been allowed through the dread of incurring the supposed risk of giving chloroform to valuable horses, dogs, &c. As has been pointed out by Mr. Hobday and others, the lower animals can be most successfully given chloroform if they are properly dealt with, if a rational method is adopted, and if the management of the anæsthetic is committed to a trained person, and not entrusted to a stable helper or a rustic, who is as incapable of giving chloroform to a horse as to a human being."

Morphia is seldom used alone; but in some cases it is used after chloroform or ether. It is certain that an animal, so far under the influence of morphia that it lies still, cannot be suffering; for the drug does not act directly on the muscles, but on the higher nervous centres. And, for the purposes of the experiment—to put the matter on the lowest ground—the animal must be kept at rest.

Lately, it was stated that "morphia acts upon dogs as a violent stimulant rather than as a narcotic, large doses causing excitement and convulsions." The reference is to an account, in the *British Medical Journal*, January 14, 1899, of a paper by Professor Lugaro, of Florence, on certain microscopic varicosities on the terminal filaments (dendrites) of the nerve-cells of the surface of the brain. These infinitely minute varicosities are said to contract when the brain is active or fatigued, and expand when it is at rest; and Lugaro's study of this vanishing-point of structure is the last word, at present, on the physical changes in sleep and unconsciousness. He used various anæsthetics and narcotics in his experim not so much to allay pain, for the experiment hardly be called painful—the animals were kill an instantaneous method of injection—but tha nerve-cells of the brain might be caught and fix the moment of contraction or expansion of the cosities of their terminal filaments. The purp the chloroform, ether, morphia, and chloral, th used, was to produce diverse conditions, suc obtain during cerebral action or inaction. T was no operation save that necessary for the inje into a vessel, and then instantaneous death animals that had been excited by morphia, as men and women are excited by it, the brain under the microscope still registered the mental at the moment of death. It happens, now and a that a dog is not influenced by morphia, is ex not narcotised, by it. But this is altogether e tional; an animal in such a condition could n used for experiment; and the physiologist has anæsthetics. Except in these rare cases, animals morphia well, and are profoundly influenced by it

Curare is not an anæsthetic under the Act. 1875–76, the evidence as to its action was some unsettled; but most of the witnesses held that it only on the motor system, and had no anæst influence. It was therefore ruled out by the and its use was thus defined in the present year (1 by the Home Secretary :—

"It is illegal to use curare as an anæsthetic. It is often used in addition to anæsthetics, for very good reasons; and, as it does not render an anæsthetised animal sensitive, it would be absurd to forbid its use."

Some of those who are opposed to all experiments on animals say that the operation is done under chloroform or ether—what they call "a whiff of chloroform"—and the animal is then subjected to horrible tortures heightened by curare. But, apart from the fact that the internal organs, even in man, are so little sensitive to touch that they may be called insensitive, and apart from the fact that morphia is combined with curare, there is evidence that curare, in such doses as are given in those few cases where it is used, acts not only on the motor system but also on the sensory system :—

"It is quite true that curare in small doses has the effect of paralysing the motor nerves without affecting the nerves of sense; but in such doses as are used in the laboratory it paralyses both sets of nerves, and this has actually been proved on man, as there have been cases of accidental curare poisoning in men who recovered, and in whom sensation has been totally abolished, while the action of the drug was apparent. Moreover, curare is nowadays not used alone, but is always used in combination with morphia, ether, chloroform, or other anæsthetics." (Prof. Rüffer, *Liberty Review*, October, 1893.)

"Much indignation has been felt about the use of curare, and the Act of 1876 expressly forbids its use as an anæsthetic. When it is used, it must be supplemented with some other drug to relieve pain. A good deal of misconception exists as to the actual physiological effect of curare, or woorali, or oorali, as it is variously called. It is the arrow poison of Guiana. It undoubtedly shows its effects first upon the muscles and their nerves. It kills by arresting respiration, by paralysing the respiratory muscles. It is a powerful poison, and unless respiration is maintained artificially the animal dies asphyxiated. Claude Bernard believed that it did not in any way affect the sensory nerves, and he described in theatrical terms the animal as being unable to stir, but suffering horrible torture. Tennyson unfortunately committed himself in a rash moment to the support of this view, speaking of it as the 'hellish woorali.' It is satisfactory to be told now that before his death he repented of his mistake, and said so to his greatest medical friends. It is pretty certainly known now that Claude Bernard was wrong, and that, though curare acts first upon the motor nerves, it also, though less rapidly, paralyses the sensory nerves, always supposing that by artificial respiration the animal is kept alive long enough for the less rapid effect to be produced. It would be out of place here to give the experimental evidence which satisfies physiologists upon this point. One case only is known to have occurred in which the full influence of curare could be studied upon a human being, and in which at the same time the presence or absence of anæsthetic effect could be noted. The case is reported by Mr. Joseph White, late of Nottingham, and a former President of the British Medical Association. A servant-girl accidentally transfixed her arm with a poisoned arrow while dusting a trophy of Indian arms in her master's hall. The arrow was withdrawn within two minutes, and the girl was seen by Mr. White half an hour later. She was then collapsed, and was breathing very badly. Artificial

> respiration was kept up, aided by faradisation. The wound was freely excised along its entire length. Two hours later reaction set in, and the patient gradually recovered. On regaining consciousness, she expressed the utmost surprise at seeing the wound in her arm, as she had felt nothing of the operation. She had, in fact, been unconscious from within half an hour of the poison. Had Claude Bernard's dictum been correct, she ought, though paralysed as to her muscles, to have been throughout the whole time conscious and sensitive. Probably the truth is that, like all other nerve-poisons, the effect of curare varies with the dose. The muscular nerves are the first affected, then the sensory, and finally the central nervous system. As a matter of fact, however, morphia or some other narcotic is always given in addition to curare when it is used in laboratory work in England." (*Edinburgh Review*, July, 1899.)

Here are two very definite statements of the action of curare: one by Prof. Rüffer, who was in 1893 Hon. Secretary of the Institute of Preventive Medicine; the other by a writer who seems to speak from experience.

Seven years ago, we had a good instance how these things are misrepresented. At the Church Congress at Folkestone, October, 1892, Mr. Horsley called attention to a book entitled "The Nine Circles," in the following words:—

> "In the book, all the experiments are grouped by Miss Cobbe as English and Foreign respectively. I have taken the trouble to collect, from this gospel of Bishop Barry

and Canon Wilberforce, all the experiments in which cutting operations are described as having been performed by English scientists, and in which I knew anæsthetics to have been employed. These experiments are twenty-six in number. In all of them, chloroform, ether, or other anæsthetic agent, was employed. But of these twenty-six cases, Miss Cobbe does not mention this fact at all in twenty, and only states it without qualification in two out of the remaining six. When we inquire into these twenty omissions in the twenty-six cases, we find in the original that again and again Miss Cobbe has, in making her extracts, had directly under her eyes the words 'chloroform,' 'ether,' 'etherised,' 'chloroformed,' 'anæsthetised,' 'during every experiment the animal has been deeply under the influence of an anæsthetic,' and so forth." (*The Standard*, October 7, 1892.)

The "Nine Circles" was compiled *for* Miss Cobbe, not *by* her; it was "planned and compiled by her direction." Mr. Berdoe was "urgently requested by her to point out to her any scientific errors or possible inadvertent misrepresentations of fact, and correct or expunge them." And he "carefully read through the proof-sheets." Miss Cobbe wrote the preface, and her name is on the title-page. The book was withdrawn at once after the Church Congress, and a revised edition was issued. At the present time, by reason of a division in the ranks of the Victoria Street Society, Miss Cobbe is editor of the *Abolitionist*, and Mr. Berdoe of the *Zoophilist*.

ACT 39 AND 40 VIC. c. 77

III

REPORTS OF THE GOVERNMENT INSPECTOR FOR ENGLAND AND SCOTLAND

The annual Reports of the Inspectors under the Act can be procured from Messrs. Eyre and Spottiswoode, Government Publishers, East Harding Street, Fleet Street, E.C. For want of space, only the three last published Reports for England and Scotland can be put here. But the following sentences from the 1890 Report are to be noted :—

> "In my visits of inspection to the various licensed places I am accustomed to examine all the animals minutely and individually, and I desire to state emphatically that it has never fallen to my lot to see a single animal which appeared to be in bodily pain. As regards the nature of the experiments, 765 were physiological, 976 were pathological, and 361 were therapeutic or pharmacological.
>
> "It is made a condition of the license that licensees shall furnish the Secretary of State with a copy of all published writings which contain details of experimental work. From these writings, as well as from personal observation as inspector, I am able to give a list of some of the chief subjects which have occupied the attention of licensees, and concerning the importance of which there can hardly be two opinions. In the domain of pathology, investigations have been made concerning tuberculosis, cancer, diphtheria, pneumonia, tetanus, acute necrosis, malaria, lead-poisoning, rabies, distemper, grouse disease, anthrax, 'black quarter,' 'pink eye,' &c. In the department of physiology, the questions of animal heat, circulation, respiration, secretion,

and the action of the central nervous system have b investigated; while among the therapeutical questi which have been examined are the actions of chlorofo morphia, nicotine, salicylic acid, strophanthus, and m other bodies which are new or less widely known, toge with investigations into the protective and other po of the products of bacteria and ferments. The amo of patient labour bestowed by the licensees upon t investigations is very great, and can hardly be imagine those who are not conversant with modern method research."

The Report for 1896.

Sir,

I have the honour to submit the following Repor Experiments performed in England and Scotland du the year 1896, under the Act 39 and 40 Vict. c. including :—

I. The Names of all Persons who have Licenses or Special Certificates during part of the Year; together with a Statemen the Registered Places at which the Lice were valid, and of the Persons who signed Applications for Licenses and granted Cer cates under the Act.

II. The Total Number of Experiments perfor during 1896, classified and arranged accordin their general Nature.

Report.

The names of all those persons who held licenses du 1896 will be found in Tables I. and II. The t number of licensees was 236, of whom 70 perfor no experiments.

The names of all those "licensed places" to w licensees were accredited are given in the tables. All licensees were restricted to the licensed place or places specified on their licenses, with the exception of those who were permitted to perform inoculation experiments in places other than a "licensed place," with the object of studying outbreaks of disease among animals in remote districts.

Tables I. and II. afford evidence,—

1. That licenses and certificates have been granted and allowed only upon the recommendation of persons of high scientific standing;
2. That the licensees are persons who, by their training and education, are fitted to undertake experimental work and to profit by it;
3. That all experimental work has been conducted in suitable places.

Table III. shows the number and the nature of the experiments performed by each licensee mentioned in Table I., specifying whether these experiments were done under the license alone or under any special certificate, so that the reader may judge which experiments (if any) were of a painful nature.

Table III. is divided into two parts, A and B, for the purpose of separating experiments of the nature of inoculations and hypodermic injections, or similar proceedings, from the rest. In each of the preceding reports which I have had the honour to make, I have drawn attention to the fact that the only experiments performed without anæsthetics are of the nature of inoculations or hypodermic injections, but in order to lessen the chance of any misapprehension on this matter I have placed these experiments in a class by themselves.

The process of inoculation is inadequately provided for in the Act of Parliament.

It would be cruel, rather than otherwise, to anæsthetise an animal before subjecting it to the trivial operation o prick with a needle, and yet the wording of the Ac such that the administration of anæsthetics can, in no c be dispensed with except by a Certificate (A) stating "insensibility cannot be produced without necess frustrating the objects" of such experiments. Notw standing that the wording of Certificate A is not wh applicable to the circumstances, it is nevertheless allo for inoculations.

The rapidly increasing knowledge of diseases cause inoculable organisms has necessitated the study of life history of such organisms by inoculation experim and other measures.

Inoculation is also largely used for the diagnosis disease in man and animals; to determine the necessi otherwise of surgical interference; and to decide whe valuable herds of animals shall be sacrificed or preserve

The discovery of antitoxins has led to their prepara on a large scale; but, as these remedies cannot be s and effectually used upon human beings without b previously tested upon rodents, the preparation antitoxins has necessitated a large number of inocula experiments.

The large increase of inoculations and allied exp ments which has been noticeable for the last few yea likely to continue.

Among the diseases a knowledge of which has b increased by inoculation experiments may be mentio tubercle, diphtheria, plague, cholera, small-pox, ent fever, septicæmia, puerperal fever, anthrax, ple pneumonia, swine fever, glanders, tetanus, silk-w disease, chicken-cholera, cattle plague, tse-tse fly dise snake-bite, &c.

The total number of experiments included in T III. (A) is 1,516.

Of these there were performed,—

Under license alone...	969
„ Certificate C	184
„ Certificate B	188
„ Certificate B + EE	175

In experiments performed under the license alone, or under Certificate C, the animal suffers no pain, because complete anæsthesia is maintained from before the commencement of the experiment until the animal is killed.

In experiments performed under Certificate B (or EE or F linked with B) the animal is anæsthetised during the operation, but is allowed to recover. These operations, in order to ensure success, are necessarily done with as much care as are similar operations upon the human subject, and the wounds being dressed antiseptically no pain results during the healing process.

Table III. (B) is devoted entirely to inoculations and hypodermic injections and some few other proceedings. It includes 5,984 experiments whereof there were performed,—

Under Certificate A	5,217
„ Certificate A + E ...	67
„ Certificate A + F ...	13
„ Certificate B	687

Nearly all the experiments under B included in this table have been inoculations made (under anæsthetics upon rodents) with the object of diagnosing rabies; the public having largely acted upon the advice printed upon the back of dog-licenses, which is to the following effect:—

> "If a dog suspected of being rabid is killed after it has bitten any person or animal, a veterinary surgeon should be requested to forward the spinal cord to the Brown Institution, Wandsworth-road (or some other licensed institution), in order that

> it may be ascertained with certainty whether the animal was suffering from rabies."

The licensees, as usual, have been loyal to the spirit of the Act. There were only two cases in which the letter of the Act was doubtfully complied with. These may be quoted as showing the difficulties of interpreting the Act in relation to inoculations.

The first case was that of a licensee who holds a Certificate A (dispensing with anæsthetics) for the inoculation of guinea-pigs with tuberculous matter. In his annual return he reported four inoculations (as performed under A) for which an anæsthetic was administered. It was necessary to take notice of this, because Certificate A is never allowed, except for proceedings so slight as to cause no appreciable pain. This gentleman has explained to me that anæsthetics were used because it was necessary to ensure perfect tranquillity while a minute incision was made in the skin, but that after the recovery from the anæsthetic the animals never afforded any evidence of discomfort. This being the case, it is possible that the experiment might have been performed under the license alone, but it clearly could not be allowed under Certificate A as used in relation to inoculations.

The second case was that of a gentleman who holds a license only, and who returned four experiments which consisted in the attempt (which failed) to give ringworm to four mice by applying the fungus, which is the cause of the disease, to the back of the animals by a few bloodless scratches without anæsthetics. It would be cruel, rather than otherwise, to administer an anæsthetic for such a proceeding. No experiment under the license alone, however, can be performed without an anæsthetic, and the licensee held no certificate enabling him to dispense with anæsthetics. It might possibly be contended that such a proceeding is not "an experiment calculated to give pain" within the meaning of the Act. This, however, is a question which has to be decided by the licensee and those who sign his application for a license. These experiments have been included in Table III. B, and have been placed in column A.

During the year the usual inspections of licensed places have been made by Sir James Russell and myself, and have been severally reported.

I have the honour to be, Sir,
Your obedient Servant,
G. V. Poore, M.D.
Inspector.

The Rt. Hon. Sir Matthew White Ridley,
Bart., M.P., Her Majesty's Secretary
of State for the Home Department.

26 *March*, 1897.

The Report for 1897.

Those paragraphs in the 1897 Report which also occur in the 1896 Report need not be again put here. The total number of Licensees was 224, of whom 61 performed no experiments. There was thus a decrease of 12 in the number of licensees. The total number of experiments included in Table III. (A) was 1462. There was thus a decrease of 54 in the number of experiments other than inoculations, injections, or similar proceedings. The total number of experiments included in Table III. (B) was 7,360. The Report says:—

"Table III. (B) is devoted entirely to inoculations and hypodermic injections, and some few other proceedings.

It includes 7,360 experiments, whereof there were performed :—

Under	Certificate A	6,799
„	Certificates A and E	111
„	Certificates A and F	14
„	Certificate B	436

"Nearly all the experiments under B included in this table have been inoculations made (under anæsthetics upon rodents) with the object of diagnosing rabies ; the public having largely acted upon the advice printed upon the back of dog-licenses, which is to the following effect :—'If a dog suspected of being rabid is killed after it has bitten any person or animal, a veterinary surgeon should be requested to forward the spinal cord to the Brown Institution, Wandsworth Road (or some other licensed institution), in order that it may be ascertained with certainty whether the animal was suffering from rabies.'

"In the past year there were seven instances of licensees inadvertently overstepping their powers under the Act. The word 'inadvertently' is used because in each case the facts were reported in good faith by the licensees themselves, and in each case they expressed their great regret at the inadvertence.

"Two licensees omitted to make the usual application for the renewal of their licenses at the end of 1896, and only discovered this omission when the time came for sending in their annual return for 1897 ; strictly speaking these two licenses were non-existent during 1897, but nevertheless the holders of them have been included in the accompanying Tables.

"Two licensees slightly exceeded the number of experiments allowed by a Certificate.

"One licensee performed four experiments under anæsthetics, though he only held Certificate A, which dispenses with their use.

"Two licensees acting conjointly gave hypodermic injections of drugs without anæsthetics, but without holding Certificate A. These have been placed under Certificate A.

"During the year the usual inspections of licensed places have been made by Sir James Russell and myself, and have been severally reported.

"I have the honour to be, Sir,
"Your obedient Servant,
"G. V. Poore, M.D.,
"*Inspector.*

"*The Rt. Hon. Sir Matthew White Ridley,*
Bart., M.P., Her Majesty's Secretary of
State for the Home Department.

"23 *March*, 1898."

The Report for 1898.

(Ordered to be printed June 8, 1899.)

"The total number of licensees during 1898 was 234, of whom 61 performed no experiments.

"The total number of experiments included in Table III. A is 1,511.

"Of these, there were performed—

Under License alone	889
,, Certificate C	179
,, Certificate B	207
,, Certificates B and EE	236

"Table III. B is devoted entirely to inoculations and hypodermic injections and some few other proceedings. It includes 7,640 experiments, whereof there were performed—

Under Certificate A	7,263
" Certificates A and E	46
" Certificates A and F	24
" Certificate B	307

"Nearly all the experiments under Certificate B included in this table have been inoculations made (under anæsthetics upon rodents) with the object of diagnosing rabies; the public having largely acted upon the advice printed upon the back of dog-licenses.

"During the past three years, the number of experiments included in Table III. A has shown little variation (1,516, 1,462, 1,511), while those included in Table III. B have increased (5,984, 7,360, 7,640). Many of these latter experiments are performed in the course of professional duty for the diagnosis of disease, the preparation of antitoxins, the testing of water, and so forth.

"It may be mentioned that during the past year 43,000 doses of diphtheria antitoxin have been issued from two institutions. The inoculations under Certificate B (Table III. B), mainly for the diagnosis of rabies, show a marked decrease in the last three years (687, 436, 307), owing to the decrease of rabies.

"Two licensees overstepped (each by one experiment) the number of experiments allowed by the Certificate under which they were working. A suitable caution was administered in each case.

"During the year, the usual inspections of licensed places have been made by Sir James Russell and myself, and have been severally reported."

IV

Official Statements

The working of the Act is subjected to ceaseless *espionage* both inside and outside Parliament. Candidates at elections are heckled over it; bullying letters are written to Her Majesty's Ministers; scientific journals are ransacked to find evidence for "The Cause"; black-lists of men to be boycotted are published; and people are asked to give nothing to the big hospitals with schools, and everything to one or two little hospitals without schools. Nothing much comes of it all: but it may be worth while to put here some recent statements, made with authority, as to the administration of the Act. They are taken, that their accuracy may be above suspicion, from the *Zoophilist*.

1

In reply to a deputation opposing the registration of the British Institute of Preventive Medicine, the Home Secretary said, in 1896:—

> "I have been most careful in inquiring from the inspectors how they conduct their visits. They are surprise visits—nearly all surprise visits—and I get a great deal of

information as to the results and the carrying on of these experiments which is not made public, in order to satisfy me, as having a very responsible position in the matter, that there is no abuse; and I really do believe that, granting you are to have experiments of this kind at all—which is sanctioned by Parliament—they are most carefully watched and guarded now, and that there is not that amount of abuse which in some quarters it is thought there is. I am convinced of that, at all events." (*Zoophilist*, August 1, 1896.)

II

From the *Zoophilist*, August 2, 1897: "Our Cause in Parliament."

"In the House of Commons, on the 8th of July, Mr. John Ellis (Nottingham, Rushcliffe), asked the Secretary for the Home Department whether the figures for experiments on living animals contained in Return No. 239 of this Session were obtained from the licensees who performed them, and in that case whether any steps were taken to verify their accuracy; whether each of the 'licensed places' was inspected during the year to which the return related, and how many of them more than once; whether any of the visits of inspection were surprise visits, and, if so, how many; and whether he had personally satisfied himself that the licenses and certificates were all issued only to such places and persons and with such objects as were contemplated by the Cruelty to Animals Act, 1876?

"Mr. Collings, Under Secretary for the Home Department, replied: Yes, the returns are obtained from the licensees, and the check, of course, upon them is supplied by the visits of the inspectors, which, with a few exceptions, are paid without notice. Four registered places at which no licenses were in force, and the laboratory attached to the Board of Agriculture, which was only registered on the 1st of December, were unvisited during the year. Five places were visited once only, eight twice, twenty-five three times, two four times, three five times, and one six times. No licensee was found during any of these visits to be exceeding his powers. The answer to the last paragraph of the question is in the affirmative.

"In the House of Commons, on the 18th of July, Mr. Weir (Ross and Cromarty) asked the Secretary of State for the Home Department whether he had yet been able to institute the promised inquiry into the allegations made by Dr. E. Berdoe in regard to the use of curare in the practice of vivisection; and, if so, would he state the result of his inquiry?

"Sir M. W. Ridley (Home Secretary): Yes, I have made full inquiry into the allegations contained in the letter and statement which the hon. member forwarded to me, and find that they are absolutely baseless. The experiments referred to were performed on animals under full chloroform anæsthesia; the morphia, to which alone allusion was made in the published account of the experiments, being used in addition. Curare was used, but not as an anæsthetic."

In reply to a further question, the Home Secretary said, "Curare is prohibited by law from being used as an anæsthetic, and I am satisfied that it is not so used." Two days later: "As I have already stated, I am satisfied that curare is not used as an anæsthetic. There are cases, however, in which its use, along with the anæsthetic, is indispensable for the success of the investigation; but its use does not make the anæsthetised animal sensible to pain."

III

From the *Zoophilist*, March 1, 1897. "The Official Returns. Questions in Parliament." (Questions relating to the two irregularities reported in the 1896 report.)

"The Home Secretary said: The irregularities consisted, in the one case, in the licensee performing an operation on a cat without having the necessary certificate; in the other case, in the licensee performing two experiments necessitating a certificate which he had omitted to obtain. In the first case, the licence was revoked and not regranted until after a period of three months and a half, and steps were taken to prevent a recurrence of the irregularity. In the second case, the consideration of the application for a renewal of the license was deferred for a month. In neither case was it thought desirable to take further proceedings."

IV

From the *Zoophilist*, April 1, 1897. "More Questions on the Returns as to Vivisection, &c."

"In the House of Commons, on Friday, March 12th, Mr. MacNeil asked the Secretary of State for the Home Department whether in view of the fact that the number of experiments performed in the year 1895 on the bodies of living animals in these countries, amounting in all to 4,679, of which 3,119 were performed under special certificates dispensing with anæsthetics, the term 'experiment' meant the whole series of experiments carried out on a particular line of research, and that 200 or 300 animals are at times used in a single experiment, while 80 or 90 is a common number; whether there is any record kept of the number of animals used in the 4,679 experiments of 1895; and whether he will, under the powers conferred on him by 39 and 40 Vic. c. 77 s. 9, direct that the vivisectors' Return for 1896 will state the number of animals used in each experiment?

"The Home Secretary: The hon. member is under an entire misapprehension.[1] The number of animals used does not exceed the number of experiments given in the return."

IV a

In reply to further questions from Mr. MacNeil, on March 12th and 23rd, the Home Secretary made the following statements:—

"The inspectors both visit registered premises during the performance of these experiments and see the bodies of animals upon which these experiments have been performed. Certificate A is never allowed except for inoculations, and similar trivial operations, and in every case a condition is attached to prevent unnecessary pain. The safeguards against the infliction of unnecessary pain are the character of the persons to whom licenses are given, the careful inquiry that is made by the Home Office beforehand, and lastly the stringent conditions under which licenses are given and certificates allowed, and which it is the duty of the inspectors to see are properly observed.

"The inspectors have been appointed by my predecessors without regard to their advocacy of or opposition to the system established by statute, under which experiments may be performed on living animals. If occasion arises, I shall pursue the same policy. The scientific knowledge required in an inspector implies a knowledge of experiments on animals, and I am satisfied that the inspection is carried out with the strictest regard to the laws and to considerations of humanity. I am persuaded that you cannot possibly examine and tell whether operations are conducted according to law unless you employ professional gentlemen who know something about the matter."

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[1] This gross "misapprehension" is repeated by a writer in the *Bradford Observer*, July 12, 1898, who says: "Any one casually reading the report (1897) would imagine that each experiment was on the body of a single animal. It is nothing of the kind. An experiment is a series of investigations in some particular branch, and sometimes twenty, thirty, or forty animals are sacrificed in the one experiment." This idiotic letter is reprinted in the *Zoophilist* for August 1, 1898, under the heading, "Our Cause in the Press," without comment.

V

From the *Zoophilist*, August 1, 1898, p. 74: "Breaches of the Law by Vivisectors."

"In the House of Commons on Tuesday, the 6th July, Sir Barrington Simeon (Southampton) asked the Secretary of State for the Home Department whether his attention had been drawn to the last report of the inspector under the Act relating to experiments on living animals; whether he had observed that seven licensees confessed to having committed offences against the law, of which two consisted in persons going on vivisecting in 1897 without the requisite license; and that the inspector having treated these two persons in the same way as licensed persons, condoned their offences; would he state who these persons were, and whether any remonstrance, reprimand, or other communication had been or would be addressed to them?

"Sir M. W. Ridley (Lancashire, Blackpool): Yes, certainly, I am aware of the facts stated in the inspector's report to myself. The nature of the irregularities referred to is shown in the report, and it will be seen that in every case they arose from inadvertence. It is not the fact, however, that the irregularities were condoned; letters of reproof were sent, and in some cases severer measures taken. No good object would, I think, be served by publishing the names."

V a

"In the House of Commons on the 11th of July, the matter was carried further by Mr. John Ellis (Nottingham, Rushcliffe), who asked the Secretary of State for the Home Department what were the severer measures which he stated had been taken in respect of the persons who were reported by the inspector as having committed breaches of the Cruelty to Animals Act, 1876, by performing painful experiments on living animals without the necessary licences or certificates?

"Sir M. W. Ridley (Lancashire, Blackpool).—Temporary suspension of and refusal to renew licenses.

"Mr. John Ellis asked the Secretary of State for the Home Department whether he could state or lay upon the table the terms of the conditions and regulations attached by the Home Office to the licences and certificates granted to persons for the performance of painful experiments on living animals under the Cruelty to Animals Act 1876?

"Sir M. W. Ridley.—The conditions are not always the same, but may vary according to the nature of the investigation. It is hardly possible, therefore, for me to state all the conditions attached to licences and certificates. The most important conditions, however (besides the limitations as to place, time, and number of experiments), and the conditions most frequently imposed, are those as to reporting and the use of antiseptics. The latter condition is that the animals are to be treated with strict antiseptic precautions, and, if these fail and pain results, they are to be killed immediately under anæsthetics. The reporting conditions are, in brief, that a written record, in a prescribed form, is to be kept of every experiment, and is to be open for examination by the inspector; that a report of all experiments is to be forwarded to the inspector; and that any published account of an experiment is to be transmitted to the Secretary of State. Another condition requires the immediate destruction under anæsthetics of an animal in which severe pain has been induced, after the main result of the experiment has been attained.

"Mr. MacNeill (Donegal, S.) asked whether it was a fact that since the Act was passed in 1876 there had been no public prosecution under the Act?

"Sir M. W. Ridley.—I am not aware of that.

"Mr. MacNeill.—Well, I am. (Laughter.)

"In the House of Commons on Friday, July 22nd, Mr. J. G. Swift MacNeill put further questions to the Home Secretary, which ran as follows:—Whether his attention had been directed to the greater frequency of the admitted breaches of the law by vivisectors; and to the circumstances that in the return for 1897 Dr. Poore, the inspector, states that illegal experiments, performed admittedly by persons without the necessary licences and certificates, have been recorded as performed by persons holding those licences and certificates, and whether Dr. Poore has been asked to give any explanation. How many inspections of places licensed for vivisection have been reported during 1897? Were these inspections carried on during experiments, or were the bodies of the vivisected animals subsequently examined? Are there any inspections of experiments by certificated operators in unregistered places?

"Sir M. W. Ridley, in reply, said: There were two such cases in each of the years 1894–96, and seven in 1897, but all arose from inadvertence, and were not, in my opinion, of a serious character, and certainly were not fitting cases for prosecution. There has only been one prosecution under the Act, and in that case the proceedings were dismissed. It is the case that two of the licensees (by what I am satisfied was mere inadvertence) omitted to apply for renewal of their licences. This is stated on page 5 of the report. It is also stated on page 7 that the list of licensees contains the names of these two gentlemen. The licences would certainly have been renewed if the ordinary application had been made. I see no objection to this course having been adopted. Dr. Poore paid sixty-one visits of inspection to licensed places in 1897, and Sir James Russell sixty-eight. Some of these visits took place during the performance of experiments, and many animals that had been experimented upon were seen by the inspector. The only experiments performed elsewhere than at registered places are inoculation operations in connection with the diseases of cattle, and inspection in such cases is deemed unnecessary and does not take place. With regard to the publication of the names of persons who have performed illegal experiments, I do not think it necessary or right that such publication should take place when the illegality has not been of so serious a nature as to call for the institution of legal proceedings.

"Mr. MacNeill.—Will the right hon. gentleman take care to give public notice that the Vivisection Act of 1876 is a dead letter?

"No answer was returned."

VI

The *Zoophilist* of Feb. 1, 1899, contains an account of a meeting held at Plymouth on Dec. 20, 1898.

The Chairman read replies from the Home Secretary touching a proposed new Bill relating to experiments on animals. In a letter explaining the objects of this Bill, it had been pointed out that it would "make it illegal to operate for scientific purposes upon a living animal before first putting that animal under a state of complete anæsthesia." To this the Home Secretary replied :—

> "This is the law already, unless the operator holds a special certificate from the Secretary of State dispensing with anæsthetics. Such special certificates are granted only for inoculations, feeding, and similar procedures involving no cutting. The animal has to be killed under anæsthetics if it be in pain as soon as the result of the experiment is ascertained. If the new law abolishes these certificates, it will put an end to the preparation and testing of anti-toxines and protective sera, as well as the most efficacious mode of studying infective diseases, and to the necessary practice of diagnostic inoculation."

The second object of the Bill was to "make it obligatory on the vivisector to destroy the animal before recovering from anæsthesia." On this point the Home Secretary's reply was :—

> "This is also law already, unless the operator has a special certificate. These certificates are granted on condition that antiseptic precautions are used ; and if these fail and pain continues after the anæsthetics have ceased to operate, the animal is immediately killed painlessly."

Another object of the Bill was "to make it illegal to use curare." To this the Home Secretary replied :—

"It is illegal to use curare as an anæsthetic. It is often used in addition to anæsthetics for very good reasons, and as it does not render an anæsthetised animal sensitive, it would be absurd to forbid its use."

These passages from the *Zoophilist* show clearly that the administration of the Act is carefully watched: and to them may be added here some portion of three amazing letters, published in the *Zoophilist* of Oct. 1, 1898. They are from the Hon. Secretary of the National Anti-Vivisection Society to three of Her Majesty's Ministers: the First Lord of the Treasury, the Home Secretary, and the President of the Board of Agriculture:—

I

". . . . We are very anxious to receive from you an open assurance that you will not use your great position to assist in the endowment of physiological research, which, as the law is now administered, means the endowment of the torture of animals. Should we be so unfortunate as to be left by you without such an open assurance, we shall feel it our duty to employ the strength and resources of this Society in an endeavour to prevent your return to Parliament at the next election. We know of a large and increasing number of your constituents who are ready, in the unfortunate event of your being unable to reassure them as to your attitude in the matter of endowing torture, to place humanity above party politics."

II

"SIR,—No reply having been received by me to my letter to Mr. Cunynghame of the 7th of July, I have now to inform you that this Society will feel it to be its duty to use every means in its power to prevent your return to Parliament at the next election, and as a protest against your having sheltered two persons who broke the law by vivisecting without licences for a whole year, from the legitimate penalties provided by the Act 39 and 40 Vic. c. 77. When the law of the land provides that certain penalties should follow breaches of that law, and the Home Secretary will neither exact those penalties himself by prosecuting the law breakers, nor permit others to do so, a time has certainly come for some protest to be made in a manner that will at least command attention."

III

"Sir,—In view of your having permitted vivisection of a very painful character to be carried on at the public expense in a laboratory attached to the office over which you preside, this Society, as representing a great body of humane persons to whom the torture of animals appears entirely unjustifiable, feels bound to protest against your action in the only way that will certainly command your attention. And, accordingly, we beg leave to inform you that at the next election the forces of this Society will be used with the utmost vigour to prevent your return to Parliament. We know of many, and shall no doubt soon secure more of your constituents, pledged to place humanity above party, and vote against you on the next occasion that you present yourself."

The Victoria Street Society is now more than twenty years old. It had on its side some of the best men in England—poets, statesmen, peers spiritual, peers temporal, great artists, great writers—what has it done? It has spent large sums of money on its literature, has spread branches all over the Empire, promoted petitions, held meetings, interfered at elections, gone again and again to Parliament; it has bullied hospitals, and Her Majesty's ministers, and men of science; it has addressed itself to the whole world—*Les mains sont vides aujourd'hui, mais la bouche peut être pleine de promesses.* It has won a number of small victories, most of them at debating societies; but its two chief victories have been won over itself. For it has at last decided that it will cease, for the present, to oppose inoculation experiments; and it has come, at last, to a good understanding with the Society for the Prevention of Cruelty to Animals.

But this book is not concerned with the Victoria Street Society; only with the results of experiments on animals, and with the Act. It was decided, and with authority, that it should be written for general reading, should be published without reserve, and should not be anonymous. To write a "medical book" for general reading is hazardous work—*Utcunque jam jacta est alea: spes mea in amore veritatis et candore doctorum animorum.*

APPENDIX

NOTE TO CHAPTER IV. (p. 81).

The *Lancet*, Sept. 23rd, mentions that the Hackney Vestry this year sent to the Jenner Institute of Preventive Medicine one hundred samples of milk, obtained in the Hackney District, to be tested for tubercle-bacilli. The report from the Institute stated that "a series of microscopic examinations was made from each sample; but such a direct examination does not yield satisfactory results. The only reliable test is by means of inoculation experiments; and these were carried out with each sample of the milk. Seventeen samples were found to contain tubercle-bacilli of virulent character."

NOTE TO CHAPTER IX. (p. 149).

1. For reports on the present plague at Oporto, from Dr. de Vicente and Dr. Mendoza, see *Lancet*, Sept. 6 and 20, 1899.

2. "A Dalziel's telegram from Bombay states that the Viceroy and his staff will shortly visit the plague

and famine stricken centres. Prior to starting every one of the party will be inoculated against the plague." (*Daily Chronicle*, Oct. 17, 1899.)

3. "It is reported that a modified form of Haffkine's plague-prophylactic has been produced, which does not give rise to the illness and suffering accompanying inoculation hitherto. Experiments are still being conducted, and it is perhaps premature to say that they have been successful. It has up to the present been believed that a good reaction (*i.e.*, fever, pain, &c.) is necessary to ensure full protection. The illness, though temporary, caused by plague-inoculation is no doubt a very serious drawback to it. The weekly returns of plague are getting worse and worse—3,684 deaths this week against 2,687 in the previous seven days. Poona city returns the appalling mortality of 1,103 deaths—a rate of over 400 per 1,000 per annum." (*Lancet*, Special Correspondent in India, Sept. 9, 1899.)

4. Dr. Hornabrook's report from the Dhárwár Plague Hospital (*Lancet*, Aug. 26, 1899), seems to prove that in those cases where inoculation has failed the disease is less dangerous to life. During August–December, 1898, the mortality was 61·86 for cases that had not been inoculated, 29·4 for the once inoculated, and 26·31 for the twice inoculated.

5. The present rush for plague-serum is putting a heavy strain on the resources of the Institutes that supply it :—

APPENDIX

i. *Paris.* "The preparation of anti-plague sen being rapidly proceeded with; up to the present tim Institute has supplied it, in response to all the very n rous requests which have come from Portugal, S Italy, and Turkey, without encroaching on the re kept in readiness for Paris and the departments." (*L* Sept. 16, 1899.)

ii. *India.* "The spread of plague westward to and Portugal seems to have excited more or less ge alarm, and I hear that an unprecedented deman suddenly arisen for the plague prophylactic fluid. Government of India have been asked the cost of supp from 50,000 to 100,000 doses, and the earliest da which this quantity could be despatched. It is desired to know if in case of need 50,000 doses a could be sent to London. Russia desires to obtain a siderable stock for Port Arthur. Italy has been ma inquiries for home use; and also Portugal, in ord inoculate at Mozambique. The present laboratory Government House, Parel, Bombay, and has only rec been fitted up by the Government of India. A 10,000 doses a day can be turned out, but it is tho that still further enlargements will be required if demand should increase beyond this amount." (*L* Sept. 23, 1899.)

NOTE TO CHAPTER XI. (p. 174).

The following account of the work of the Ma Expedition was published in *The Outlook*, Oct. 1899:—

"*The Colonisation of the Tropics.*

"The return of the triumphant Malaria Expeditic the Liverpool school this week in the steamship *Fa* marks an epoch in the progress of the colonisation of the tropics. Until the discovery of the malarial parasite in the body of the mosquito by Major Ross, scarcely two years ago, we knew little more of the origin of that scourge of the tropics under its score of names, 'Jungle-fever,' 'Swamp-evil,' 'Coast-fever,' 'African blight,' than of that of the Aurora Borealis. That it prevailed in marshes, in hot climates, and could—sometimes—be cured by quinine was about the practical sense of our knowledge. Ross's discovery, confirmed as it quickly was by Bignami and Grassi, opened an entire horizon of new possibilities. The vague and hopeless problem of the prevention of malaria became narrowed down to the definite and hopeful one of the prevention of mosquitoes, or at least of mosquito-bites. And it is not too much to say that the expedition now returning has brought this down from a theoretic possibility to a mere question of time and expense.

"The important points established by the Expedition are three. First, that in Africa, as in India and Italy, it is one small and not very abundant species or sub-family of mosquitoes, *Anopheles*, that is the sole bearer of the infection. This was proved by the double test of finding this species abundant in regions specially affected by malaria, and of discovering the parasite in the tissues of individual insects captured. And as *Anopheles* may be distinguished at a glance from the common 'skeeter' by the fact of its perching with its body projecting spike-fashion at right angles from the wall instead of parallel with it, as in all other species, its detection during its resting period, the day-time, is easy even for the non-expert eye. Second, that as this species fortunately flies only for about an hour before and two hours after sunset, keeping behind mosquito-barred or curtained windows during these hours is an absolute protection against malarial infection. This was most luckily—for every one except the victim—exemplified by the experience of one of the physicians wh slept one night without mosquito-curtains, and was th only member of the party who had the slightest touch o malaria during their nearly three months' stay in one o the most malarious regions in the wòrld. The thir point is the definite 'locating' of the class of poo in which *Anopheles* breeds. Fortunately he is a mos exacting and fastidious person. He will only breed i pools that are permanent, or at least exist during th greater part of the year. This is the reason why he i only about one-tenth as common as his harmless, bu most exasperating cousin *Culex*, who will breed in an rain-puddle, water-butt, or even sardine-tin half-filled b a tropical shower. But this pool must not be too permanent, otherwise it would be invaded by minnows, wh regard the eggs and larvæ of mosquitoes as the choicest of delicacies, so that any pondlet stocked with fish, or even where they can penetrate during floods or at high water, is barred to *Anopheles*. Lastly, in order to feel really at home, he must have an abundant growth o algæ or slime-weeds, for upon these the young larvæ feed greedily. To find a pool which satisfies all three of these nice and exacting requirements is most mercifully difficult, so that the result is that '*Anopheles* pools' may number only a dozen or so in an entire neighbourhood.

"Major Ross declares that an expert eye 'soon comes to recognise them at first glance, by instinct,' and as a quart of kerosene will absolutely 'sterilise' a hundred square yards of pool surface, it ought, with a little time and patience, to be perfectly feasible to rid a whole tropical region of this great bar to colonisation."

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